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<b>(21) International Application Number:</b> PCT/NZ99/00051 <b>(22) International Filing Date:</b> 29 April 1999 (29.04.99)  <b>(30) Priority Data:</b> 09/069,726                      29 April 1998 (29.04.98)                      US 09/188,930                      9 November 1998 (09.11.98)                      US  <b>(71) Applicant:</b> GENESIS RESEARCH AND DEVELOPMENT CORPORATION LIMITED [NZ/NZ]; 1 Fox Street, Parnell, Auckland (NZ).  <b>(72) Inventors:</b> STRACHAN, Lorna; 11/50 Livingstone Street, Coss Bay, Auckland (NZ). SLEEMAN, Matthew; 19 Derwent Crescent, Titirangi, Auckland (NZ). WATSON, James, Douglas; 769 Riddell Road, St Heliers, Auckland (NZ). ONRUST, Rene; 21 Duart Avenue, Mt Albert, Auckland (NZ). KUMBLE, Anand; 4 Stanton Terrace, Lynfield, Auckland (NZ). MURISON, James, Greg; 24 Calgary Street, Sandringham, Auckland (NZ).  <b>(74) Agents:</b> BENNETT, Michael, Roy et al.; Russell McVeagh West-Walker, Mobil on the Park, 157 Lambton Quay, Wellington (NZ).		<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> POLYNUCLEOTIDES ISOLATED FROM SKIN CELLS AND METHODS FOR THEIR USE  <b>(57) Abstract</b>  Isolated polynucleotides encoding polypeptides expressed in mammalian skin cells are provided, together with expression vectors and host cells comprising such isolated polynucleotides. Methods for the use of such polynucleotides and polypeptides are also provided.		

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## POLYNUCLEOTIDES ISOLATED FROM SKIN CELLS AND METHODS FOR THEIR USE

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### Technical Field of the Invention

This invention relates to polynucleotides encoding polypeptides, polypeptides expressed in skin cells, and their use in therapeutic methods.

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### Background of the Invention

The skin is the largest organ in the body and serves as a protective cover. The loss of skin, as occurs in a badly burned person, may lead to death owing to the absence of a barrier against infection by external microbial organisms, as well as loss of body temperature and body fluids.

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Skin tissue is composed of several layers. The outermost layer is the epidermis which is supported by a basement membrane and overlies the dermis. Beneath the dermis is loose connective tissue and fascia which cover muscles or bony tissue. The skin is a self-renewing tissue in that cells are constantly being formed and shed. The deepest cells of the epidermis are the basal cells, which are enriched in cells capable of replication. Such replicating cells are called progenitor or stem cells. Replicating cells in turn give rise to daughter cells called 'transit amplifying cells'. These cells undergo differentiation and maturation into keratinocytes (mature skin cells) as they move from the basal layer to the more superficial layers of the epidermis. In the process, keratinocytes become cornified and are ultimately shed from the skin surface. Other cells in the epidermis include melanocytes which synthesize melanin, the pigment responsible for protection against sunlight. The Langerhans cell also resides in the epidermis and functions as a cell which processes foreign proteins for presentation to the immune system.

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The dermis contains nerves, blood and lymphatic vessels, fibrous and fatty tissue. Within the dermis are fibroblasts, macrophages and mast cells. Both the epidermis and dermis are penetrated by sweat, or sebaceous, glands and hair follicles. Each strand of

hair is derived from a hair follicle. When hair is plucked out, the hair re-grows from epithelial cells directed by the dermal papillae of the hair follicle.

When the skin surface is breached, for example in a wound, the stem cells proliferate and daughter keratinocytes migrate across the wound to reseal the tissues. The skin cells therefore possess genes activated in response to trauma. The products of these genes include several growth factors, such as epidermal growth factor, which mediate the proliferation of skin cells. The genes that are activated in the skin, and the protein products of such genes, may be developed as agents for the treatment of skin wounds. Additional growth factors derived from skin cells may also influence growth of other cell types. As skin cancers are a disorder of the growth of skin cells, proteins derived from skin that regulate cellular growth may be developed as agents for the treatment of skin cancers. Skin derived proteins that regulate the production of melanin may be useful as agents which protect skin against unwanted effects of sunlight.

Keratinocytes are known to secrete cytokines and express various cell surface proteins. Cytokines and cell surface molecules are proteins which play an important role in the inflammatory response against infection and also in autoimmune diseases affecting the skin. Genes and their protein products that are expressed by skin cells may thus be developed into agents for the treatment of inflammatory disorders affecting the skin.

Hair is an important part of a person's individuality. Disorders of the skin may lead to hair loss. Alopecia areata is a disease characterized by the patchy loss of hair over the scalp. Total baldness is a side effect of drug treatment for cancer. The growth and development of hair are mediated by the effects of genes expressed in skin and dermal papillae. Such genes and their protein products may be usefully developed into agents for the treatment of disorders of the hair follicle.

New treatments are required to hasten the healing of skin wounds, to prevent the loss of hair, enhance the re-growth of hair or removal of hair, and to treat autoimmune and inflammatory skin diseases more effectively and without adverse effects. More effective treatments of skin cancers are also required. There thus remains a need in the art for the identification and isolation of genes encoding proteins expressed in the skin, for use in the development of therapeutic agents for the treatment of disorders including those associated with skin.



Summary of the Invention

The present invention provides polypeptides expressed in skin cells, together with polynucleotides encoding such polypeptides, expression vectors and host cells comprising such polynucleotides, and methods for their use.

In specific embodiments, isolated polynucleotides are provided that comprise a DNA sequence selected from the group consisting of: (a) sequences recited in SEQ ID NO: 1-14, 45-48, 64-68, 77-89, 118, 119, 198-231, 239-249, 254-274, 349-372 and 399-405; (b) complements of the sequences recited in SEQ ID NO: 1-14, 45-48, 64-68, 77-89, 118, 119, 198-231, 239-249, 254-274, 349-372 and 399-405; (c) reverse complements of the sequences recited in SEQ ID NO: 1-14, 45-48, 64-68, 77-89, 118, 119, 198-231, 239-249, 254-274, 349-372 and 399-405; (d) reverse sequences of the sequences recited in SEQ ID NO: 1-14, 45-48, 64-68, 77-89, 118, 119, 198-231, 239-249, 254-274, 349-372 and 399-405; (e) sequences having a 99% probability of being the same as a sequence of (a)-(d); and (f) sequences having at least 50%, 75% or 90% identity to a sequence of (a)-(d).

In further embodiments, the present invention provides isolated polypeptides comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409, together with isolated polynucleotides encoding such polypeptides. Isolated polypeptides which comprise at least a functional portion of a polypeptide comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409; and (b) sequences having 50%, 75% or 90% identity to a sequence of SEQ ID NO: 120-197, 275-348, 373-398 and 406-409 are also provided.

In related embodiments, the present invention provides expression vectors comprising the above polynucleotides, together with host cells transformed with such vectors.

In a further aspect, the present invention provides a method of stimulating keratinocyte growth and motility, inhibiting the growth of epithelial-derived cancer cells,

inhibiting angiogenesis and vascularization of tumors, or modulating the growth of blood vessels in a subject, comprising administering to the subject a composition comprising an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 187, 196, 342, 343, 395, 397, and 398; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 187, 196, 342, 343, 395, 397, and 398.

Methods for modulating skin inflammation in a subject are also provided, the methods comprising administering to the subject a composition comprising an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 338 and 347; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 338 and 347. In an additional aspect, the present invention provides methods for stimulating the growth of epithelial cells in a subject. Such methods comprise administering to the subject a composition comprising an isolated polypeptide including an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 129 and 348; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 129 and 348. In yet a further aspect, methods for inhibiting the binding of HIV-1 to leukocytes, for the treatment of an inflammatory disease or for the treatment of cancer in a subject are provided, the methods comprising administering to the subject a composition comprising an isolated polypeptide including an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 340, 344, 345 and 346; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 340, 344, 345 and 346.

As detailed below, the isolated polynucleotides and polypeptides of the present invention may be usefully employed in the preparation of therapeutic agents for the treatment of skin disorders.

The above-mentioned and additional features of the present invention, together with the manner of obtaining them, will be best understood by reference to the following more detailed description. All references disclosed herein are hereby incorporated herein by reference in their entirety as if each was incorporated individually.

### Brief Description of the Drawings

Fig. 1 shows the results of a Northern analysis of the distribution of huTR1 mRNA in human tissues. Key: He, Heart; Br, Brain; Pl, Placenta; Lu, Lung; Li, Liver; SM, Skeletal muscle; Ki, Kidney; Sp, Spleen; Th, Thymus; Pr, Prostate; Ov, Ovary.

Fig. 2 shows the results of a MAP kinase assay of muTR1a and huTR1a. MuTR1a (500ng/ml), huTR1a (100ng/ml) or LPS (3pg/ml) were added as described in the text.

Fig. 3 shows the stimulation of growth of neonatal foreskin keratinocytes by muTR1a.

Fig. 4 shows the stimulation of growth of the transformed human keratinocyte cell line HaCaT by muTR1a and huTR1a.

Fig. 5 shows the inhibition of growth of the human epidermal carcinoma cell line A431 by muTR1a and huTR1a.

Fig. 6 shows the inhibition of IL-2 induced growth of concanavalin A-stimulated murine splenocytes by KS2a.

Fig. 7 shows the stimulation of growth of rat intestinal epithelial cells (IEC-18) by a combination of KS3a plus apo-transferrin.

Fig. 8 illustrates the oxidative burst effect of TR-1 (100 ng/ml), muKS1 (100 ng/ml), SDF1 $\alpha$  (100 ng/ml), and fMLP (10  $\mu$ M) on human PBMC.

Figure 9 shows the chemotactic effect of muKS1 and SDF-1 $\alpha$  on THP-1 cells.

Figure 10 shows the induction of cellular infiltrate in C3H/HeJ mice after intraperitoneal injections with muKS1 (50  $\mu$ g), GV14B (50  $\mu$ g) and PBS.

Figure 11 demonstrates the induction of phosphorylation of ERK1 and ERK2 in CV1/EBNA and HeLa cell lines by huTR1a.

Figure 12 shows the huTR1 mRNA expression in HeLa cells after stimulation by muTR1, huTR1, huTGF $\alpha$  and PBS (100 ng/ml each).

Figure 13 shows activation of the SRE by muTR1a in PC-12 (Fig. 13a) and HaCaT (Fig. 13b) cells.

Figure 14 shows the inhibition of huTR1a mediated growth on HaCaT cells by an antibody to the EGF receptor.

#### Detailed Description of the Invention

In one aspect, the present invention provides polynucleotides that were isolated from mammalian skin cells. As used herein, the term "polynucleotide" means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and RNA molecules, both sense and anti-sense strands. The term comprehends cDNA, genomic DNA, recombinant DNA and wholly or partially synthesized nucleic acid molecules. A polynucleotide may consist of an entire gene, or a portion thereof. A gene is a DNA sequence that codes for a functional protein or RNA molecule. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all operable anti-sense fragments. Anti-sense polynucleotides and techniques involving anti-sense polynucleotides are well known in the art and are described, for example, in Robinson-Benion et al., "Anti-sense Techniques," *Methods in Enzymol.* 254(23):363-375, 1995; and Kawasaki et al., *Artific. Organs* 20 (8):836-848, 1996.

Identification of genomic DNA and heterologous species DNAs can be accomplished by standard DNA/DNA hybridization techniques, under appropriately stringent conditions, using all or part of a cDNA sequence as a probe to screen an appropriate library. Alternatively, PCR techniques using oligonucleotide primers that are designed based on known genomic DNA, cDNA and protein sequences can be used to amplify and identify genomic and cDNA sequences. Synthetic DNAs corresponding to the identified sequences and variants may be produced by conventional synthesis methods. All the polynucleotides provided by the present invention are isolated and purified, as those terms are commonly used in the art.

In specific embodiments, the polynucleotides of the present invention comprise a DNA sequence selected from the group consisting of sequences provided in SEQ ID NO: 1-119, 198-274, 349-372 and 399-405, and variants of the sequences of SEQ ID NO: 1-119, 198-274, 349-372 and 399-405. Polynucleotides that comprise complements of such DNA sequences, reverse complements of such DNA sequences, or reverse

sequences of such DNA sequences, together with variants of such sequences, are also provided.

The definition of the terms "complement," "reverse complement," and "reverse sequence," as used herein, is best illustrated by the following example. For the sequence  
5 5' AGGACC 3', the complement, reverse complement, and reverse sequence are as follows:

complement	3' TCCTGG 5'
reverse complement	3' GGTCCT 5'
reverse sequence	5' CCAGGA 3'.

10 In another aspect, the present invention provides isolated polypeptides encoded, or partially encoded, by the above polynucleotides. As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins, wherein the amino acid residues are linked by covalent peptide bonds. The term "polypeptide encoded by a polynucleotide" as used herein, includes polypeptides  
15 encoded by a polynucleotide which comprises a partial isolated DNA sequence provided herein. In specific embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409, as well as variants of such sequences.

Polypeptides of the present invention may be produced recombinantly by  
20 inserting a DNA sequence that encodes the polypeptide into an expression vector and expressing the polypeptide in an appropriate host. Any of a variety of expression vectors known to those of ordinary skill in the art may be employed. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide.  
25 Suitable host cells include prokaryotes, yeast, and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, insect, yeast, or a mammalian cell line such as COS or CHO. The DNA sequences expressed in this manner may encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof.

In a related aspect, polypeptides are provided that comprise at least a functional  
30 portion of a polypeptide having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 120-197, 275-348, 373-398, 406-409,

and variants thereof. As used herein, the "functional portion" of a polypeptide is that portion which contains the active site essential for affecting the function of the polypeptide, for example, the portion of the molecule that is capable of binding one or more reactants. The active site may be made up of separate portions present on one or more polypeptide chains and will generally exhibit high binding affinity.

Functional portions of a polypeptide may be identified by first preparing fragments of the polypeptide by either chemical or enzymatic digestion of the polypeptide, or by mutation analysis of the polynucleotide that encodes the polypeptide and subsequent expression of the resulting mutant polypeptides. The polypeptide fragments or mutant polypeptides are then tested to determine which portions retain biological activity, using, for example, the representative assays provided below.

Portions and other variants of the inventive polypeptides may also be generated by synthetic or recombinant means. Synthetic polypeptides having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems, Inc. (Foster City, California), and may be operated according to the manufacturer's instructions. Variants of a native polypeptide may be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (Kunkel, T., *Proc. Natl. Acad. Sci. USA* 82:488-492, 1985). Sections of DNA sequence may also be removed using standard techniques to permit preparation of truncated polypeptides.

In general, the polypeptides disclosed herein are prepared in an isolated, substantially pure, form. Preferably, the polypeptides are at least about 80% pure, more preferably at least about 90% pure, and most preferably at least about 99% pure. In certain preferred embodiments, described in detail below, the isolated polypeptides are

incorporated into pharmaceutical compositions or vaccines for use in the treatment of skin disorders.

As used herein, the term "variant" comprehends nucleotide or amino acid sequences different from the specifically identified sequences, wherein one or more nucleotides or amino acid residues is deleted, substituted, or added. Variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant sequences (polynucleotide or polypeptide) preferably exhibit at least 50%, more preferably at least 75%, and most preferably at least 90% identity to a sequence of the present invention. The percentage identity is determined by aligning the two sequences to be compared as described below, determining the number of identical residues in the aligned portion, dividing that number by the total number of residues in the inventive (queried) sequence, and multiplying the result by 100.

Polynucleotide or polypeptide sequences may be aligned, and percentage of identical nucleotides in a specified region may be determined against another polynucleotide or polypeptide, using computer algorithms that are publicly available. Two exemplary algorithms for aligning and identifying the similarity of polynucleotide sequences are the BLASTN and FASTA algorithms. The alignment and similarity of polypeptide sequences may be examined using the BLASTP and algorithm. BLASTX and FASTX algorithms compare nucleotide query sequences translated in all reading frames against polypeptide sequences. The BLASTN, BLASTP and BLASTX algorithms are available on the NCBI anonymous FTP server (<ftp://ncbi.nlm.nih.gov>) under /blast/executables/. The FASTA and FASTX algorithms are available on the Internet at the ftp site <ftp://ftp.virginia.edu/pub/>. The FASTA algorithm, set to the default parameters described in the documentation and distributed with the algorithm, may be used in the determination of polynucleotide variants. The readme files for FASTA and FASTX v1.0x that are distributed with the algorithms describe the use of the algorithms and describe the default parameters. The use of the FASTA and FASTX algorithms is also described in Pearson, WR and Lipman, DJ, "Improved Tools for Biological Sequence Analysis," *PNAS* 85:2444-2448, 1988; and Pearson WR, "Rapid and Sensitive Sequence Comparison with FASTP and FASTA," *Methods in Enzymology* 183:63-98, 1990.

The BLASTN algorithm version 2.0.4 [Feb-24-1998], set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of polynucleotide variants according to the present invention. The BLASTP algorithm version 2.0.4, set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of polypeptide variants according to the present invention. The use of the BLAST family of algorithms, including BLASTN, BLASTP and BLASTX is described at NCBI's website at URL <http://www.ncbi.nlm.nih.gov/BLAST/newblast.html> and in the publication of Altschul, Stephen F., *et al.*, "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs," *Nucleic Acids Res.* 25:3389-3402, 1997.

The following running parameters are preferred for determination of alignments and similarities using BLASTN that contribute to the E values and percentage identity for polynucleotides: Unix running command with default parameters thus: `blastall -p blastn -d embldb -e 10 -G 0 -E 0 -r 1 -v 30 -b 30 -i queryseq -o results`; and parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero invokes default behavior) [Integer]; -r Reward for a nucleotide match (blastn only) [Integer]; -v Number of one-line descriptions (V) [Integer]; -b Number of alignments to show (B) [Integer]; -i Query File [File In]; -o BLAST report Output File [File Out]

Optional. The following running parameters are preferred for determination of alignments and similarities using BLASTP that contribute to the E values and percentage identity for polypeptides: `blastall -p blastp -d swissprot -e 10 -G 1 -E 11 -r 1 -v 30 -b 30 -i queryseq -o results`; and the parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero invokes default behavior) [Integer]; -v Number of one-line descriptions (v) [Integer]; -b Number of alignments to show (b) [Integer]; -I Query File [File In]; -o BLAST report Output File [File Out]

Optional.

The "hits" to one or more database sequences by a queried sequence produced by BLASTN, BLASTP, FASTA, or a similar algorithm, align and identify similar portions of sequences. The hits are arranged in order of the degree of similarity and the length of



sequence overlap. Hits to a database sequence generally represent an overlap over only a fraction of the sequence length of the queried sequence.

The percentage similarity of a polynucleotide or polypeptide sequence is determined by aligning polynucleotide and polypeptide sequences using appropriate algorithms, such as BLASTN or BLASTP, respectively, set to default parameters; identifying the number of identical nucleic or amino acids over the aligned portions; dividing the number of identical nucleic or amino acids by the total number of nucleic or amino acids of the polynucleotide or polypeptide of the present invention; and then multiplying by 100 to determine the percentage similarity. By way of example, a queried polynucleotide having 220 nucleic acids has a hit to a polynucleotide sequence in the EMBL database having 520 nucleic acids over a stretch of 23 nucleotides in the alignment produced by the BLASTN algorithm using the default parameters. The 23 nucleotide hit includes 21 identical nucleotides, one gap and one different nucleotide. The percentage identity of the queried polynucleotide to the hit in the EMBL database is thus 21/220 times 100, or 9.5%. The similarity of polypeptide sequences may be determined in a similar fashion.

The BLASTN and BLASTX algorithms also produce "Expect" values for polynucleotide and polypeptide alignments. The Expect value (E) indicates the number of hits one can "expect" to see over a certain number of contiguous sequences by chance when searching a database of a certain size. The Expect value is used as a significance threshold for determining whether the hit to a database indicates true similarity. For example, an E value of 0.1 assigned to a polynucleotide hit is interpreted as meaning that in a database of the size of the EMBL database, one might expect to see 0.1 matches over the aligned portion of the sequence with a similar score simply by chance. By this criterion, the aligned and matched portions of the sequences then have a probability of 90% of being the same. For sequences having an E value of 0.01 or less over aligned and matched portions, the probability of finding a match by chance in the EMBL database is 1% or less using the BLASTN algorithm. E values for polypeptide sequences may be determined in a similar fashion using various polypeptide databases, such as the SwissProt database.

According to one embodiment, "variant" polynucleotides and polypeptides, with reference to each of the polynucleotides and polypeptides of the present invention, preferably comprise sequences having the same number or fewer nucleic or amino acids than each of the polynucleotides or polypeptides of the present invention and producing  
5 an E value of 0.01 or less when compared to the polynucleotide or polypeptide of the present invention. That is, a variant polynucleotide or polypeptide is any sequence that has at least a 99% probability of being the same as the polynucleotide or polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTN or BLASTX algorithms set at the default parameters. According to a preferred  
10 embodiment, a variant polynucleotide is a sequence having the same number or fewer nucleic acids than a polynucleotide of the present invention that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using the BLASTN algorithm set at the default parameters. Similarly, according to a preferred embodiment, a variant polypeptide is a  
15 sequence having the same number or fewer amino acids than a polypeptide of the present invention that has at least a 99% probability of being the same as the polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTP algorithm set at the default parameters.

Variant polynucleotide sequences will generally hybridize to the recited  
20 polynucleotide sequences under stringent conditions. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65 °C and two washes of 30 minutes each in 0.2X SSC, 0.1% SDS at 65 °C.

25 As used herein, the term "x-mer," with reference to a specific value of "x," refers to a polynucleotide or polypeptide, respectively, comprising at least a specified number ("x") of contiguous residues of: any of the polynucleotides provided in SEQ ID NO: 1-119, 198-274, 349-372 and 399-405; or any of the polypeptides set out in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409. The value of x may be from about 20 to about  
30 600, depending upon the specific sequence.

Polynucleotides of the present invention comprehend polynucleotides comprising at least a specified number of contiguous residues (x-mers) of any of the polynucleotides identified as SEQ ID NO: 1-119, 198-274, 349-372 and 399-405, or their variants. Polypeptides of the present invention comprehend polypeptides comprising at least a specified number of contiguous residues (x-mers) of any of the polypeptides identified as SEQ ID NO: 120-197, 275-348, 373-398, and 406-409. According to preferred embodiments, the value of  $x$  is at least 20, more preferably at least 40, more preferably yet at least 60, and most preferably at least 80. Thus, polynucleotides of the present invention include polynucleotides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer; or a 300-mer, 400-mer, 500-mer or 600-mer of a polynucleotide provided in SEQ ID NO: 1-119, 198-274, 349-372 and 399-405 or a variant of one of the polynucleotides provided in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405. Polypeptides of the present invention include polypeptides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer; or a 300-mer, 400-mer, 500-mer or 600-mer of a polypeptide provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, or a variant of one of the polynucleotides provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409.

The inventive polynucleotides may be isolated by high throughput sequencing of cDNA libraries prepared from mammalian skin cells as described below in Example 1. Alternatively, oligonucleotide probes based on the sequences provided in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405 can be synthesized and used to identify positive clones in either cDNA or genomic DNA libraries from mammalian skin cells by means of hybridization or polymerase chain reaction (PCR) techniques. Probes can be shorter than the sequences provided herein but should be at least about 10, preferably at least about 15 and most preferably at least about 20 nucleotides in length. Hybridization and PCR techniques suitable for use with such oligonucleotide probes are well known in the art (see, for example, Mullis, *et al.*, *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich, ed., *PCR Technology*, Stockton Press: NY, 1989; (Sambrook, J, Fritsch, EF and Maniatis, T, eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring

Harbor Laboratory Press, Cold Spring Harbor: New York, 1989). Positive clones may be analyzed by restriction enzyme digestion, DNA sequencing or the like.

In addition, DNA sequences of the present invention may be generated by synthetic means using techniques well known in the art. Equipment for automated  
5 synthesis of oligonucleotides is commercially available from suppliers such as Perkin Elmer/Applied Biosystems Division (Foster City, California) and may be operated according to the manufacturer's instructions.

Since the polynucleotide sequences of the present invention have been derived from skin, they likely encode proteins that have important roles in growth and  
10 development of skin, and in responses of skin to tissue injury and inflammation as well as disease states. Some of the polynucleotides contain sequences that code for signal sequences, or transmembrane domains, which identify the protein products as secreted molecules or receptors. Such protein products are likely to be growth factors, cytokines, or their cognate receptors. Several of the polypeptide sequences have more than 25%  
15 similarity to known biologically important proteins and thus are likely to represent proteins having similar biological functions.

In particular, the inventive polypeptides have important roles in processes such as: induction of hair growth; differentiation of skin stem cells into specialized cell types; cell migration; cell proliferation and cell-cell interaction. The polypeptides are important in  
20 the maintenance of tissue integrity, and thus are important in processes such as wound healing. Some of the disclosed polypeptides act as modulators of immune responses, especially since immune cells are known to infiltrate skin during tissue insult causing growth and differentiation of skin cells. In addition, many polypeptides are immunologically active, making them important therapeutic targets in a whole range of  
25 disease states not only within skin, but also in other tissues of the body. Antibodies to the polypeptides of the present invention and small molecule inhibitors related to the polypeptides of the present invention may also be used for modulating immune responses and for treatment of diseases according to the present invention.

In one aspect, the present invention provides methods for using one or more of the  
30 inventive polypeptides or polynucleotides to treat disorders in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human.

In this aspect, the polypeptide or polynucleotide is generally present within a pharmaceutical composition or a vaccine. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above sequences (or variants thereof), and a physiologically acceptable carrier. Vaccines may  
5 comprise one or more of the above polypeptides and a non-specific immune response amplifier, such as an adjuvant or a liposome, into which the polypeptide is incorporated.

Alternatively, a vaccine or pharmaceutical composition of the present invention may contain DNA encoding one or more polypeptides as described above, such that the polypeptide is generated *in situ*. In such vaccines and pharmaceutical compositions, the  
10 DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, and bacterial and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminator signal). Bacterial delivery systems involve the administration of a bacterium (such as  
15 *Bacillus-Calmette-Guerin*) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other poxvirus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic, or defective, replication competent virus. Techniques for incorporating DNA into such expression systems are well known in the  
20 art. The DNA may also be "naked," as described, for example, in Ulmer, *et al.*, *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

Routes and frequency of administration, as well as dosage, will vary from  
25 individual to individual. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intradermal, intramuscular, intravenous, or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg per  
30 kg of host, and preferably from about 100 pg to about 1  $\mu$ g per kg of host. Suitable dose

sizes will vary with the size of the patient, but will typically range from about 0.1 ml to about 5 ml.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax, or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactic galactide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Any of a variety of adjuvants may be employed in the vaccines derived from this invention to non-specifically enhance the immune response. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a non-specific stimulator of immune responses, such as lipid A, *Bordetella pertussis*, or *M. tuberculosis*. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Freund's Complete Adjuvant (Difco Laboratories, Detroit, Michigan), and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, New Jersey). Other suitable adjuvants include alum, biodegradable microspheres, monophosphoryl lipid A, and Quil A.

The polynucleotides of the present invention may also be used as markers for tissue, as chromosome markers or tags, in the identification of genetic disorders, and for the design of oligonucleotides for examination of expression patterns using techniques well known in the art, such as the microarray technology available from Synteni (Palo Alto, California). Partial polynucleotide sequences disclosed herein may be employed to obtain full length genes by, for example, screening of DNA expression libraries using hybridization probes or PCR primers based on the inventive sequences.

The polypeptides provided by the present invention may additionally be used in assays to determine biological activity, to raise antibodies, to isolate corresponding ligands or receptors, in assays to quantitatively determine levels of protein or cognate

corresponding ligand or receptor, as anti-inflammatory agents, and in compositions for skin, connective tissue and/or nerve tissue growth or regeneration.

### Example 1

#### 5 ISOLATION OF CDNA SEQUENCES FROM SKIN CELL EXPRESSION LIBRARIES

The cDNA sequences of the present invention were obtained by high-throughput sequencing of cDNA expression libraries constructed from specialized rodent or human skin cells as shown in Table 1.

10

Table 1

<u>Library</u>	<u>Skin cell type</u>	<u>Source</u>
DEPA	dermal papilla	rat
SKTC	keratinocytes	human
HNFF	neonatal foreskin fibroblast	human
15 MEMS	embryonic skin	mouse
KSCL	keratinocyte stem cell	mouse
<u>TRAM</u>	<u>transit amplifying cells</u>	<u>mouse</u>

These cDNA libraries were prepared as described below.

#### 20 cDNA Library from Dermal Papilla (DEPA)

Dermal papilla cells from rat hair vibrissae (whiskers) were grown in culture and the total RNA extracted from these cells using established protocols. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, 25 California), according to the manufacturer's specifications. A cDNA expression library was then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

#### cDNA Library from Keratinocytes (SKTC)

Keratinocytes obtained from human neonatal foreskins (Mitra, R and Nikoloff, B 30 in *Handbook of Keratinocyte Methods*, pp. 17-24, 1994) were grown in serum-free KSFM (BRL Life Technologies) and harvested along with differentiated cells ( $10^8$  cells). Keratinocytes were allowed to differentiate by addition of fetal calf serum at a final

concentration of 10% to the culture medium and cells were harvested after 48 hours. Total RNA was isolated from the two cell populations using TRIzol Reagent (BRL Life Technologies) and used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene). cDNAs expressed in differentiated keratinocytes were enriched by using a  
5 PCR-Select cDNA Subtraction Kit (Clontech, Palo Alto, California). Briefly, mRNA was obtained from either undifferentiated keratinocytes ("driver mRNA") or differentiated keratinocytes ("tester mRNA") and used to synthesize cDNA. The two populations of cDNA were separately digested with *RsaI* to obtain shorter, blunt-ended molecules. Two tester populations were created by ligating different adaptors at the  
10 cDNA ends and two successive rounds of hybridization were performed with an excess of driver cDNA. The adaptors allowed for PCR amplification of only the differentially expressed sequences which were then ligated into T-tailed pBluescript (Hadjeb, N and Berkowicz, GA, *BioTechniques* 20:20-22 1996), allowing for a blue/white selection of cells containing vector with inserts. White cells were isolated and used to obtain plasmid  
15 DNA for sequencing.

cDNA library from human neonatal fibroblasts (HNFF)

Human neonatal fibroblast cells were grown in culture from explants of human neonatal foreskin and the total RNA extracted from these cells using established protocols. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies,  
20 Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, California), according to the manufacturer's specifications. A cDNA expression library was then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA library from mouse embryonic skin (MEMS)

25 Embryonic skin was micro-dissected from day 13 post coitum Balb/c mice. Embryonic skin was washed in phosphate buffered saline and mRNA directly isolated from the tissue using the Quick Prep Micro mRNA purification kit (Pharmacia, Sweden). The mRNA was then used to prepare cDNA libraries as described above for the DEPA library.

30 cDNA library from mouse stem cells (KSCL) and transit amplifying (TRAM) cells

Pelts obtained from 1-2 day post-partum neonatal Balb/c mice were washed and



incubated in trypsin (BRL Life Technologies) to separate the epidermis from the dermis. Epidermal tissue was disrupted to disperse cells, which were then resuspended in growth medium and centrifuged over Percoll density gradients prepared according to the manufacturer's protocol (Pharmacia, Sweden). Pelleted cells were labeled using  
5 Rhodamine 123 (Bertoncello I, Hodgson GS and Bradley TR, *Exp Hematol.* 13:999-1006, 1985), and analyzed by flow cytometry (Epics Elite Coulter Cytometry, Hialeah, Florida). Single cell suspensions of rhodamine-labeled murine keratinocytes were then labeled with a cross reactive anti-rat CD29 biotin monoclonal antibody (Pharmingen, San Diego, California; clone Ha2/5). Cells were washed and incubated with anti-mouse  
10 CD45 phycoerythrin conjugated monoclonal antibody (Pharmingen; clone 30F11.1, 10ug/ml) followed by labeling with streptavidin spectral red (Southern Biotechnology, Birmingham, Alabama). Sort gates were defined using listmode data to identify four populations: CD29 bright rhodamine dull CD45 negative cells; CD29 bright rhodamine bright CD45 negative cells; CD29 dull rhodamine bright CD45 negative cells; and CD29  
15 dull rhodamine dull CD45 negative cells. Cells were sorted, pelleted and snap frozen prior to storage at -80°C. This protocol was followed multiple times to obtain sufficient cell numbers of each population to prepare cDNA libraries. Skin stem cells and transit amplifying cells are known to express CD29, the integrin  $\beta 1$  chain. CD45, a leucocyte specific antigen, was used as a marker for cells to be excluded in the isolation of skin  
20 stem cells and transit amplifying cells. Keratinocyte stem cells expel the rhodamine dye more efficiently than transit amplifying cells. The CD29 bright, rhodamine dull, CD45 negative population (putative keratinocyte stem cells; referred to as KSCL), and the CD29 bright, rhodamine bright, CD45 negative population (keratinocyte transit amplifying cells; referred to as TRAM) were sorted and mRNA was directly isolated  
25 from each cell population using the Quick Prep Micro mRNA purification kit (Pharmacia, Sweden). The mRNA was then used to prepare cDNA libraries as described above for the DEPA library.

cDNA sequences were obtained by high-throughput sequencing of the cDNA libraries described above using a Perkin Elmer/Applied Biosystems Division Prism 377  
30 sequencer.

Example 2CHARACTERIZATION OF ISOLATED cDNA SEQUENCES

The isolated cDNA sequences were compared to sequences in the EMBL DNA database using the computer algorithms FASTA and/or BLASTN. The corresponding  
5 predicted protein sequences (DNA translated to protein in each of 6 reading frames) were compared to sequences in the SwissProt database using the computer algorithms FASTX and/or BLASTP. Comparisons of DNA sequences provided in SEQ ID NO: 1-119 to sequences in the EMBL DNA database (using FASTA) and amino acid sequences provided in SEQ ID NO: 120-197 to sequences in the SwissProt database (using FASTX)  
10 were made as of March 21, 1998. Comparisons of DNA sequences provided in SEQ ID NO: 198-274 to sequences in the EMBL DNA database (using BLASTN) and amino acid sequences provided in SEQ ID NO: 275-348 to sequences in the SwissProt database (using BLASTP) were made as of October 7, 1998. Comparisons of DNA sequences provided in SEQ ID NO: 349-372 to sequences in the EMBL DNA database (using  
15 BLASTN) and amino acid sequences provided in SEQ ID NO: 373-398 to sequences in the SwissProt database (using BLASTP) were made as of January 23, 1999.

Isolated cDNA sequences and their corresponding predicted protein sequences were computer analyzed for the presence of signal sequences identifying secreted molecules. Isolated cDNA sequences that have a signal sequence at a putative start site  
20 within the sequence are provided in SEQ ID NO: 1-44, 198-238, 349-358, and 399. The cDNA sequences of SEQ ID NO: 1-6, 198-199, 349-352, 354, and 356-358 were determined to have less than 75% identity (determined as described above), to sequences in the EMBL database using the computer algorithms FASTA or BLASTN, as described above. The predicted amino acid sequences of SEQ ID NO: 120-125, 275-276, 373-380,  
25 and 382 were determined to have less than 75% identity (determined as described above) to sequences in the SwissProt database using the computer algorithms FASTX or BLASTP, as described above.

Further sequencing of some of the isolated partial cDNA sequences resulted in the isolation of the full-length cDNA sequences provided in SEQ ID NO: 7-14, 200-231,  
30 and 372. The corresponding predicted amino acid sequences are provided in SEQ ID NO: 126-133, 277-308, and 396, respectively. Comparison of the full length cDNA

sequences with those in the EMBL database using the computer algorithm FASTA or BLASTN, as described above, revealed less than 75% identity (determined as described above) to known sequences. Comparison of the predicted amino acid sequences provided in SEQ ID NO: 126-133 and 277-308 with those in the SwissProt database using the computer algorithms FASTX or BLASTP, as described above, revealed less than 75% identity (determined as described above) to known sequences.

Comparison of the predicted amino acid sequences corresponding to the cDNA sequences of SEQ ID NO: 15-23 with those in the EMBL using the computer algorithm FASTA database showed less than 75% identity (determined as described above) to known sequences. These predicted amino acid sequences are provided in SEQ ID NO: 134-142.

Further sequencing of some of the isolated partial cDNA sequences resulted in the isolation of full-length cDNA sequences provided in SEQ ID NO: 24-44 and 232-238. The corresponding predicted amino acid sequences are provided in SEQ ID NO: 143-163 and 309-315, respectively. These amino acid sequences were determined to have less than 75% identity, determined as described above to known sequences in the SwissProt database using the computer algorithm FASTX.

Isolated cDNA sequences having less than 75% identity to known expressed sequence tags (ESTs) or to other DNA sequences in the public database, or whose corresponding predicted protein sequence showed less than 75% identity to known protein sequences, were computer analyzed for the presence of transmembrane domains coding for putative membrane-bound molecules. Isolated cDNA sequences that have either one or more transmembrane domain(s) within the sequence are provided in SEQ ID NO: 45-63, 239-253, 359-364, 400-402. The cDNA sequences of SEQ ID NO: 45-48, 239-249, 359-361, and 363 were found to have less than 75% identity (determined as described above) to sequences in the EMBL database, using the FASTA or BLASTN computer algorithms. Their predicted amino acid sequences provided in SEQ ID NO: 164-167, 316-326, 383, 385-388 and 407-408 were found to have less than 75% identity, determined as described above, to sequences in the SwissProt database using the FASTX or BLASTP database.

Comparison of the predicted amino acid sequences corresponding to the cDNA sequences of SEQ ID NO: 49-63 and 250-253 with those in the SwissProt database showed less than 75% identity (determined as described above) to known sequences. These predicted amino acid sequences are provided in SEQ ID NO: 168-182 and  
5 327-330.

Using automated search programs to screen against sequences coding for molecules reported to be of therapeutic and/or diagnostic use, some of the cDNA sequences isolated as described above in Example 1 were determined to encode predicted protein sequences that appear to be family members of known protein families. A family  
10 member is here defined to have at least 25% identity in the translated polypeptide to a known protein or member of a protein family. These cDNA sequences are provided in SEQ ID NO: 64-76, 254-264, 365-369, and 403, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 183-195, 331-341, 389-393 and 409, respectively. The cDNA sequences of SEQ ID NO: 64-68, 254-264, and 365-369 show  
15 less than 75% identity (determined as described above) to sequences in the EMBL database using the FASTA or BLASTN computer algorithms. Similarly, the amino acid sequences of SEQ ID NO: 183-195, 331-341, and 389-393 show less than 75% identity to sequences in the SwissProt database.

The likely utility for each of the proteins encoded by the DNA sequences of SEQ  
20 ID NO: 64-76, 254-264, 365-369, and 403, based on similarity to known proteins, is provided below:

Table 2

## FUNCTIONS OF NOVEL PROTEINS

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS
64 372	183 396	Slit, a secreted molecule required for central nervous system development
65	184	Immunoglobulin receptor family. About 40% of leucocyte membrane polypeptides contain immunoglobulin superfamily domains
66 403	185 409	RIP protein kinase, a serine/threonine kinase that contains a death domain to mediate apoptosis
67	186	Extracellular protein with epidermal growth factor domain capable of stimulating fibroblast proliferation
68	187	Transforming growth factor alpha, a protein which binds epidermal growth factor receptor and stimulates growth and mobility of keratinocytes
69	188	DRS protein which has a secretion signal component and whose expression is suppressed in cells transformed by oncogenes
70	189	A33 receptor with immunoglobulin-like domains and is expressed in greater than 95% of colon tumors
71	190	Interleukin-12 alpha subunit, component of a cytokine that is important in the immune defense against intracellular pathogens. IL-12 also stimulates proliferation and differentiation of TH1 subset of lymphocytes
72	191	Tumor Necrosis Factor receptor family of proteins that are involved in the proliferation, differentiation and death of many cell types including B and T lymphocytes.
73	192	Epidermal growth factor family proteins which stimulate growth and mobility of keratinocytes and epithelial cells. EGF is involved in wound healing. It also inhibits gastric acid secretion.
74	193	Fibronectin Type III receptor family. The fibronectin III domains are found on the extracellular regions of cytokine receptors
75	194	Serine/threonine kinases (STK2_HUMAN) which participate in cell cycle progression and signal transduction
76	195	Immunoglobulin receptor family
254	331	Receptor with immunoglobulin-like domains and homology to A33 receptor which is expressed in greater than 95% of colon tumors
255	332	Epidermal growth factor family proteins which stimulate growth and mobility of keratinocytes and epithelial cells. EGF is involved in wound healing. It also inhibits gastric acid secretion.

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS
256	333	Serine/threonine kinases (STK2_HUMAN) which participate in cell cycle progression and signal transduction
257	334	Contains protein kinase and ankyrin domains. Possible role in cellular growth and differentiation.
258	335	Notch family proteins which are receptors involved in cellular differentiation.
259	336	Extracellular protein with epidermal growth factor domain capable of stimulating fibroblast proliferation.
260	337	Fibronectin Type III receptor family. The fibronectin III domains are found on the extracellular regions of cytokine receptors.
261	338	Immunoglobulin receptor family
262	339	ADP/ATP transporter family member containing a calcium binding site.
263	340	Mouse CXC chemokine family members are regulators of epithelial, lymphoid, myeloid, stromal and neuronal cell migration and cancers, agents for the healing of cancers, neuro-degenerative diseases, wound healing, inflammatory autoimmune diseases like psoriasis, asthma, Crohns disease and as agents for the prevention of HIV-1 of leukocytes
264	341	Nucleotide-sugar transporter family member.
365	389	Transforming growth factor betas (TGF-betas) are secreted covalently linked to latent TGF-beta-binding proteins (LTBPs). LTBPs are deposited in the extracellular matrix and play a role in cell growth or differentiation.
366	390	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
367	391	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
368	392	Cell wall protein precursor. Are involved in cellular growth or differentiation.
369	393	HT protein is a secreted glycoprotein with an EGF-like domain. It functions as a modulator of cell growth, death or differentiation.

These isolated sequences thus encode proteins that influence the growth, differentiation and activation of several cell types. They may usefully be developed as

agents for the treatment and diagnosis of skin wounds, cancers, growth and developmental defects, and inflammatory disease.

The polynucleotide sequences of SEQ ID NO: 77-117, 265-267, and 404-405 are differentially expressed in either keratinocyte stem cells (KSCL) or in transit amplified cells (TRAM) on the basis of the number of times these sequences exclusively appear in either one of the above two libraries; more than 9 times in one and none in the other (Audic S. and Claverie J-M, *Genome Research*, 7:986-995, 1997). The sequences of SEQ ID NO: 77-89, 265-267, and 365-369 were determined to have less than 75% identity to sequences in the EMBL and SwissProt databases using the computer algorithm FASTA or BLASTN, as described above. The proteins encoded by these polynucleotide sequences have utility as markers for identification and isolation of these cell types, and antibodies against these proteins may be usefully employed in the isolation and enrichment of these cells from complex mixtures of cells. Isolated polynucleotides and their corresponding proteins exclusive to the stem cell population can be used as drug targets to cause alterations in regulation of growth and differentiation of skin cells, or in gene targeting to transport specific therapeutic molecules to skin stem cells.

### Example 3

#### ISOLATION AND CHARACTERIZATION OF THE HUMAN HOMOLOG OF MUTR1

The human homolog of muTR1 (SEQ ID NO: 68), obtained as described above in Example 1, was isolated by screening 50,000 pfu's of an oligo dT primed HeLa cell cDNA library. Plaque lifts, hybridization, and screening were performed using standard molecular biology techniques (Sambrook, J, Fritsch, EF and Maniatis, T, eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor: New York, 1989). The determined cDNA sequence of the isolated human homolog (huTR1) is provided in SEQ ID NO: 118, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 196. The library was screened using an [ $\alpha$   $^{32}$ P]-dCTP labeled double stranded cDNA probe corresponding to nucleotides 1 to 459 of the coding region within SEQ ID NO: 118.

The polypeptide sequence of huTR1 has regions similar to Transforming Growth Factor-alpha, indicating that this protein functions like an epidermal growth factor (EGF).

This EGF-like protein will serve to stimulate keratinocyte growth and motility, and to inhibit the growth of epithelial-derived cancer cells. This novel gene and its encoded protein may thus be used as agents for the healing of wounds and regulators of epithelial-derived cancers.

5 Analysis of RNA transcripts by Northern Blotting

Northern analysis to determine the size and distribution of mRNA for huTR1 was performed by probing human tissue mRNA blots (Clontech) with a probe comprising nucleotides 93-673 of SEQ ID NO: 118, radioactively labeled with [ $\alpha^{32}\text{P}$ ]-dCTP. Prehybridization, hybridization, washing and probe labeling were performed as described in Sambrook, *et al.*, *Ibid.* mRNA for huTR1 was 3.5-4kb in size and was observed to be most abundant in heart and placenta, with expression at lower levels being observed in spleen, thymus prostate and ovary (Fig. 1).

The high abundance of mRNA for huTR1 in the heart and placenta indicates a role for huTR1 in the formation or maintenance of blood vessels, as heart and placental tissues have an increased abundance of blood vessels, and therefore endothelial cells, compared to other tissues in the body. This, in turn, demonstrates a role for huTR1 in angiogenesis and vascularization of tumors. This is supported by the ability of Transforming Growth Factor-alpha and EGF to induce *de novo* development of blood vessels (Schreiber, *et al.*, *Science* 232:1250-1253, 1986) and stimulate DNA synthesis in endothelial cells (Schreiber, *et al.*, *Science* 232:1250-1253, 1986), and their over-expression in a variety of human tumors.

Purification of muTR1 and huTR1

Polynucleotides 177-329 of muTR1 (SEQ ID NO: 268), encoding amino acids 53-103 of muTR1 (SEQ ID NO: 342), and polynucleotides 208-360 of huTR1 (SEQ ID NO: 269), encoding amino acids 54-104 of huTR1 (SEQ ID NO: 343), were cloned into the bacterial expression vector pProEX HT (BRL Life Technologies), which contains a bacterial leader sequence and N-terminal 6xHistidine tag. These constructs were transformed into competent XL1-Blue *E. coli* as described in Sambrook *et al.*, *Ibid.*

30 Starter cultures of these recombinant XL1-Blue *E. coli* were grown overnight at 37°C in Terrific broth containing 100 µg/ml ampicillin. This culture was spun down and



used to inoculate 500 ml culture of Terrific broth containing 100 µg/ml ampicillin. Cultures were grown until the OD<sub>595</sub> of the cells was between 0.4 and 0.8, whereupon IPTG was added to 1 mM. Cells were induced overnight and bacteria were harvested by centrifugation.

5 Both the polypeptide of muTR1 (SEQ ID NO: 342; referred to as muTR1a) and that of huTR1 (SEQ ID NO: 343; referred to as huTR1a) were expressed in insoluble inclusion bodies. In order to purify the polypeptides muTR1a and huTR1a, bacterial cell pellets were re-suspended in lysis buffer (20 mM Tris-HCl pH 8.0, 10 mM beta mercaptoethanol, 1 mM PMSF). To the lysed cells, 1% NP40 was added and the mix  
10 incubated on ice for 10 minutes. Lysates were further disrupted by sonication on ice at 95W for 4 x 15 seconds and then centrifuged for 15 minutes at 14,000 rpm to pellet the inclusion bodies.

The resulting pellet was re-suspended in lysis buffer containing 0.5% w/v CHAPS and sonicated on ice for 5-10 seconds. This mix was stored on ice for 1 hour, centrifuged  
15 at 14,000 rpm for 15 minutes at 4 °C and the supernatant discarded. The pellet was once more re-suspended in lysis buffer containing 0.5% w/v CHAPS, sonicated, centrifuged and the supernatant removed as before. The pellet was re-suspended in solubilizing buffer (6 M Guanidine HCl, 0.5 M NaCl, 20 mM Tris HCl, pH 8.0), sonicated at 95 W for 4 x 15 seconds and then centrifuged for 20 minutes at 14,000 rpm and 4 °C to remove  
20 debris. The supernatant was stored at 4 °C until use.

Polypeptides muTR1a and huTR1a were purified by virtue of the N-terminal 6x Histidine tag contained within the bacterial leader sequence, using a Nickel-Chelating Sepharose column (Amersham Pharmacia, Uppsala, Sweden) and following the manufacturer's recommended protocol. In order to refold the proteins once purified, the  
25 protein solution was added to 5x its volume of refolding buffer (1 mM EDTA, 1.25 mM reduced glutathione, 0.25 mM oxidised glutathione, 20 mM Tris-HCl, pH 8.0) over a period of 1 hour at 4 °C. The refolding buffer was stirred rapidly during this time, and stirring continued at 4 °C overnight. The refolded proteins were then concentrated by ultrafiltration using standard protocols.

Biological Activities of Polypeptides muTR1a and huTR1a

muTR1 and huTR1 are novel members of the EGF family, which includes EGF, TGF $\alpha$ , epiregulin and others. These growth factors are known to act as ligands for the EGF receptor. The pathway of EGF receptor activation is well documented. Upon  
5 binding of a ligand to the EGF receptor, a cascade of events follows, including the phosphorylation of proteins known as MAP kinases. The phosphorylation of MAP kinase can thus be used as a marker of EGF receptor activation. Monoclonal antibodies exist which recognize the phosphorylated forms of 2 MAP kinase proteins – ERK1 and ERK2.

10 In order to examine whether purified polypeptides of muTR1a and huTR1a act as a ligand for the EGF receptor, cells from the human epidermal carcinoma cell line A431 (American Type Culture Collection, No. CRL-1555, Manassas, Virginia) were seeded into 6 well plates, serum starved for 24 hours, and then stimulated with purified muTR1a or huTR1a for 5 minutes in serum free conditions. As a positive control, cells were  
15 stimulated in the same way with 10 to 100 ng/ml TGF- $\alpha$  or EGF. As a negative control, cells were stimulated with PBS containing varying amounts of LPS. Cells were immediately lysed and protein concentration of the lysates estimated by Bradford assay. 15  $\mu$ g of protein from each sample was loaded onto 12% SDS-PAGE gels. The proteins were then transferred to PVDF membrane using standard techniques.

20 For Western blotting, membranes were incubated in blocking buffer (10mM Tris-HCl, pH 7.6, 100 mM NaCl, 0.1% Tween-20, 5% non-fat milk) for 1 hour at room temperature. Rabbit anti-Active MAP kinase pAb (Promega, Madison, Wisconsin) was added to 50 ng/ml in blocking buffer and incubated overnight at 4 °C. Membranes were washed for 30 mins in blocking buffer minus non-fat milk before being incubated with  
25 anti rabbit IgG-HRP antibody, at a 1:3500 dilution in blocking buffer, for 1 hour at room temperature. Membranes were washed for 30 minutes in blocking buffer minus non-fat milk, then once for 5 minutes in blocking buffer minus non-fat milk and 0.1% Tween-20. Membranes were then exposed to ECL reagents for 2 min, and then autoradiographed for 5 to 30 min.

30 As shown in Fig. 2, both muTR1a and huTR1a were found to induce the phosphorylation of ERK1 and ERK2 over background levels, indicating that muTR1 and

huTR1 act as ligands for a cell surface receptor that activates the MAP kinase signaling pathway, possibly the EGF receptor. As shown in Fig. 11, huTR1a was also demonstrated to induce the phosphorylation of ERK1 and ERK2 in CV1/EBNA kidney epithelial cells in culture, as compared with the negative control. These assays were  
5 conducted as described above. This indicates that huTR1a acts as a ligand for a cell surface receptor that activates the MAP kinase signaling pathway, possibly the EGF receptor in HeLa and CV1/EBNA cells.

The ability of muTR1a to stimulate the growth of neonatal foreskin (NF) keratinocytes was determined as follows. NF keratinocytes derived from surgical  
10 discards were cultured in KSFM (BRL Life Technologies) supplemented with bovine pituitary extract (BPE) and epidermal growth factor (EGF). The assay was performed in 96 well flat-bottomed plates in 0.1 ml unsupplemented KSFM. MuTR1a, human transforming growth factor alpha (huTGF $\alpha$ ) or PBS-BSA was titrated into the plates and  $1 \times 10^3$  NF keratinocytes were added to each well. The plates were incubated for 5 days  
15 in an atmosphere of 5% CO<sub>2</sub> at 37°C. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 3, both muTR1a and the positive control human TGF $\alpha$  stimulated the growth of NF keratinocytes, whereas the negative control, PBS-BSA, did not.

The ability of muTR1a and huTR1a to stimulate the growth of a transformed  
20 human keratinocyte cell line, HaCaT, was determined as follows. The assay was performed in 96 well flat-bottomed plates in 0.1 ml DMEM (BRL Life Technologies) supplemented with 0.2% FCS. MuTR1a, huTR1a and PBS-BSA were titrated into the plates and  $1 \times 10^3$  HaCaT cells were added to each well. The plates were incubated for 5 days in an atmosphere containing 10% CO<sub>2</sub> at 37°C. The degree of cell growth was  
25 determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 4, both muTR1a and huTR1a stimulated the growth of HaCaT cells, whereas the negative control PBS-BSA did not.

The ability of muTR1a and huTR1a to inhibit the growth of A431 cells was determined as follows. Polypeptides muTR1a (SEQ ID NO: 342) and huTR1a (SEQ ID  
30 NO: 343) and PBS-BSA were titrated as described previously (*J. Cell. Biol.* 93:1-4, 1982) and cell death determined using the MTT dye reduction as described previously

(*J. Imm. Meth.* 93:157-165, 1986). Both muTR1a and huTR1a were found to inhibit the growth of A431 cells, whereas the negative control PBS-BSA did not (Fig. 5).

These results indicate that muTR1 and huTR1 stimulate keratinocyte growth and motility, inhibit the growth of epithelial-derived cancer cells, and play a role in angiogenesis and vascularization of tumors. This novel gene and its encoded protein may thus be developed as agents for the healing of wounds, angiogenesis and regulators of epithelial-derived cancers.

#### *Upregulation of huTR1 and mRNA expression*

HeLa cells (human cervical adenocarcinoma) were seeded in 10 cm dishes at a concentration of  $1 \times 10^6$  cells per dish. After incubation overnight, media was removed and replaced with media containing 100 ng/ml of muTR1, huTR1, huTGF $\alpha$ , or PBS as a negative control. After 18 hours, media was removed and the cells lysed in 2 ml of TRIzol reagent (Gibco BRL Life Technologies, Gaithersburg, Maryland). Total RNA was isolated according to the manufacturer's instructions. To identify mRNA levels of huTR1 from the cDNA samples, 1  $\mu$ l of cDNA was used in a standard PCR reaction. After cycling for 30 cycles, 5  $\mu$ l of each PCR reaction was removed and separated on a 1.5% agarose gel. Bands were visualized by ethidium bromide staining. As can be seen from Fig. 12, both mouse and human TR1 up-regulate the mRNA levels of huTR1 as compared with cells stimulated with the negative control of PBS. Furthermore, TGF $\alpha$  can also up-regulate the mRNA levels of huTR1.

These results indicate that TR1 is able to sustain its own mRNA expression and subsequent protein expression, and thus is expected to be able to contribute to the progression of diseases such as psoriasis where high levels of cytokine expression are involved in the pathology of the disease. Furthermore, since TGF $\alpha$  can up-regulate the expression of huTR1, the up-regulation of TR1 mRNA may be critical to the mode of action of TGF $\alpha$ .

#### *Serum response element reporter gene assay*

The serum response element (SRE) is a promoter element required for the regulation of many cellular immediate-early genes by growth. Studies have demonstrated that the activity of the SRE can be regulated by the MAP kinase signaling pathway. Two cell lines, PC12 (rat pheochromocytoma – neural tumor) and HaCaT (human transformed

keratinocytes), containing eight SRE upstream of an SV40 promotor and luciferase reporter gene were developed in-house.  $5 \times 10^3$  cells were aliquoted per well of 96 well plate and grown for 24 hours in their respective media. HaCaT SRE cells were grown in 5% fetal bovine serum (FBS) in D-MEM supplemented with 2mM L-glutamine (Sigma, St. Louis, Missouri), 1mM sodium pyruvate (BRL Life Technologies), 0.77mM L-asparagine (Sigma), 0.2mM arginine (Sigma), 160mM penicillin G (Sigma), 70mM dihydrostreptomycin (Roche Molecular Biochemicals, Basel, Switzerland), and 0.5 mg/ml geneticin (BRL Life Technologies). PC12 SRE cells were grown in 5% fetal bovine serum in Ham F12 media supplemented with 0.4 mg/ml geneticin (BRL Life Technologies). Media was then changed to 0.1% FBS and incubated for a further 24 hours. Cells were then stimulated with a titration of TR1 from 1  $\mu$ g/ml. A single dose of basic fibroblast growth factor at 100 ng/ml (R&D Systems, Minneapolis, Minnesota) or epidermal growth factor at 10 ng/ml (BRL Life Technologies) was used as a positive control. Cells were incubated in the presence of muTR1 or positive control for 6 hours, washed twice in PBS and lysed with 40  $\mu$ l of lysis buffer (Promega). 10  $\mu$ l was transferred to a 96 well plate and 10  $\mu$ l of luciferase substrate (Promega) added by direct injection into each well by a Victor<sup>2</sup> fluorimeter (Wallac), the plate was shaken and the luminescence for each well read at 3x1 sec Intervals. Fold induction of SRE was calculated using the following equation: Fold induction of SRE = Mean relative luminescence of agonist/Mean relative luminescence of negative control.

As shown in Fig. 13, muTR1 activates the SRE in both PC-12 (Fig. 13a) and HaCaT (Fig. 13b) cells. This indicates that HaCaT and PC-12 cells are able to respond to muTR1 protein and elicit a response. In the case of HaCaT cells, this is a growth response. In the case of PC-12 cells, this may be a growth, a growth inhibition, differentiation, or migration response. Thus, TR1 may be important in the development of neural cells or their differentiation into specific neural subsets. TR1 may also be important in the development and progression of neural tumors.

#### *Inhibition by the EGF receptor assay*

The HaCaT growth assay was conducted as previously described, except that modifications were made as follows. Concurrently with the addition of EGF and TR1 to the media, anti-EGF Receptor (EGFR) antibody (Promega, Madison, Wisconsin) or

negative control antibody, mouse IgG (PharMingen, San Diego, California), were added at a concentration of 62.5 ng/ml.

As seen in Fig. 14, an antibody which blocks the function of the EGFR inhibits the mitogenicity of TR1 on HaCaT cells. This indicates that the EGFR is crucial for transmission of the TR1 mitogenic signal on HaCaT cells. TR1 may bind directly to the EGF receptor. TR1 may also bind to any other members of the EGFR family – ErbB-2, -3, and/or -4 – that are capable of heterodimerizing with the EGFR.

*Sequence of splice variant of huTR1, huTR1 $\beta$*

A variant of huTR1 was isolated from the same library as huTR1 (SEQ ID NO: 118), following the same protocols. This sequence is a splice variant of huTR1 and consists of the ORF of huTR1 minus amino acids 87 to 137. This has the effect of deleting the third cysteine residue of the EGF motif and the transmembrane domain. However, cysteine residue 147 (huTR1 ORF numbering) may replace the deleted cysteine and thus the disulphide bridges are likely not affected. Therefore, huTR1 $\beta$  is a secreted form of huTR1. It functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGF $\alpha$ . The determined nucleotide sequence of the splice variant of TR1, referred to as huTR1 $\beta$ , is given in SEQ ID NO: 371 and the corresponding predicted amino acid sequence is SEQ ID NO: 395.

Example 4

IDENTIFICATION, ISOLATION AND CHARACTERIZATION OF DP3

A partial cDNA fragment, referred to as DP3, was identified by differential display RT-PCR (modified from Liang P and Pardee AB, *Science* 257:967-971, 1992) using mRNA from cultured rat dermal papilla and footpad fibroblast cells, isolated by standard cell biology techniques. This double stranded cDNA was labeled with [ $\alpha^{32}$ P]-dCTP and used to identify a full length DP3 clone by screening 400,000 pfu's of an oligo dT-primed rat dermal papilla cDNA library. The determined full-length cDNA sequence for DP3 is provided in SEQ ID NO: 119, with the corresponding amino acid sequence being provided in SEQ ID NO: 197. Plaque lifts, hybridization and screening were performed using standard molecular biology techniques.

Example 5ISOLATION AND CHARACTERIZATION OF THE  
HUMAN HOMOLOG OF muKS15 Analysis of RNA transcripts by Northern Blotting

Northern analysis to determine the size and distribution of mRNA for muKS1 (SEQ ID NO: 263) was performed by probing murine tissue mRNA blots with a probe consisting of nucleotides 268-499 of muKS1, radioactively labeled with [ $\alpha^{32}\text{P}$ ]-dCTP. Prehybridization, hybridization, washing, and probe labeling were performed as described in Sambrook, *et al.*, *Ibid.* mRNA for muKS1 was 1.6 kb in size and was observed to be most abundant in brain, lung, muscle, and heart. Expression could also be detected in lower intestine, skin, and kidney. No detectable signal was found in testis, spleen, liver, thymus, stomach.

Human homologue of muKS1

15 MuKS1 (SEQ ID NO: 263) was used to search the EMBL database (Release 50, plus updates to June, 1998) to identify human EST homologues. The top three homologues were to the following ESTs: accession numbers AA643952, HS1301003 and AA865643. These showed 92.63% identity over 285 nucleotides, 93.64% over 283 nucleotides and 94.035% over 285 nucleotides, respectively. Frame shifts were identified in AA643952 and HS1301003 when translated. Combination of all three ESTs identified  
20 huKS1 (SEQ ID NO: 270) and translated polypeptide SEQ ID NO: 344. Alignment of muKS1 and huKS1 polypeptides indicated 95% identity over 96 amino acids.

Bacterial expression and purification of muKS1 and huKS1

Polynucleotides 269-502 of muKS1 (SEQ ID NO: 271), encoding amino acids  
25 23-99 of polypeptide muKS1 (SEQ ID NO: 345), and polynucleotides 55-288 of huKS1 (SEQ ID NO: 272), encoding amino acids 19-95 of polypeptide huKS1 (SEQ ID NO: 346), were cloned into the bacterial expression vector pET-16b (Novagen, Madison, Wisconsin), which contains a bacterial leader sequence and N-terminal 6xHistidine tag. These constructs were transformed into competent XL1-Blue *E. coli* as described in  
30 Sambrook *et al.*, *Ibid.*

Starter cultures of recombinant BL 21 (DE3) *E. coli* (Novagen) containing SEQ ID NO: 271 (muKS1a) and SEQ ID NO: 272 (huKS1a) were grown in NZY broth containing 100 µg/ml ampicillin (Gibco-BRL Life Technologies) at 37°C. Cultures were spun down and used to inoculate 800 ml of NZY broth and 100 µg/ml ampicillin. 5 Cultures were grown until the OD<sub>595</sub> of the cells was between 0.4 and 0.8. Bacterial expression was induced for 3 hours with 1 mM IPTG. Bacterial expression produced an induced band of approximately 15kDa for muKS1a and huKS1a.

MuKS1a and huKS1a were expressed in insoluble inclusion bodies. In order to purify the polypeptides, bacterial cell pellets were re-suspended in lysis buffer (20 mM 10 Tris-HCl pH 8.0, 10 mM βMercaptoethanol, 1 mM PMSF). To the lysed cells, 1% NP-40 was added and the mix incubated on ice for 10 minutes. Lysates were further disrupted by sonication on ice at 95 W for 4 x 15 seconds and then centrifuged for 10 minutes at 18,000 rpm to pellet the inclusion bodies.

The pellet containing the inclusion bodies was re-suspended in lysis buffer 15 containing 0.5% w/v CHAPS and sonicated for 5-10 seconds. This mix was stored on ice for 1 hour, centrifuged at 14000 rpm for 15 minutes at 4°C and the supernatant discarded. The pellet was once more re-suspended in lysis buffer containing 0.5% w/v CHAPS, sonicated, centrifuged, and the supernatant removed as before. The pellet was re-suspended in solubilizing buffer (6 M guanidine HCl, 0.5 M NaCl, 20 mM Tris-HCl 20 pH 8.0), sonicated at 95W for 4 x 15 seconds and centrifuged for 10 minutes at 18000 rpm and 4°C to remove debris. The supernatant was stored at 4°C. MuKS1a and huKS1a were purified by virtue of the N-terminal 6x histidine tag contained within the bacterial leader sequence, using a Nickel-Chelating sepharose column (Amersham Pharmacia, Uppsala, Sweden) and following the manufacturer's protocol. Proteins were purified 25 twice over the column to reduce endotoxin contamination. In order to re-fold the proteins once purified, the protein solution was dialysed in a 4 M-2 M urea gradient in 20 mM tris-HCl pH 7.5 + 10% glycerol overnight at 4°C. The protein was then further dialysed 2x against 2 litres of 20 mM Tris-HCl pH 7.5 + 10% glycerol.

#### *Peptide sequencing of muKS1 and huKS1*

30 Bacterially expressed muKS1 and huKS1 were separated on polyacrylamide gels and induced bands of 15 kDa were identified. The predicted size of muKS1 is 9.4 kDa.



To obtain the amino acid sequence of the 15 kDa bands, 20 µg recombinant muKS1 and huKS1 was resolved by SDS-PAGE and electroblotted onto Immobilon PVDF membrane (Millipore, Bedford, Massachusetts). Internal amino acid sequencing was performed on tryptic peptides of muKS1 and huKS1 by the Protein Sequencing Unit at the University  
5 of Auckland, New Zealand.

The determined amino acid sequences for muKS1 and huKS1 are given in SEQ ID NOS: 397 and 398, respectively. These amino acid sequences confirmed that the determined sequences are identical to that predicted from the cDNA sequences. The size discrepancy has previously been reported for other chemokines (Richmond A,  
10 Balentien E, Thomas HG, Flaggs G, Barton DE, Spiess J, Bordoni R, Francke U, Derynck R, "Molecular characterization and chromosomal mapping of melanoma growth stimulatory activity, a growth factor structurally related to beta-thromboglobulin," *EMBO J.* 7:2025-2033, 1988; Liao F, Rabin RL, Yannelli JR, Koniaris LG, Vanguri P, Farber JM, "Human Nig chemokine: biochemical and functional characterization,"  
15 *J. Exp. Med.* 182:1301-1314, 1995). The isoelectric focusing point of these proteins was predicted to be 10.26 using DNASIS (HITACHI Software Engineering, San Francisco, California).

#### *Oxidative burst assay*

Oxidative burst assays were used to determine responding cell types.  $1 \times 10^7$   
20 PBMC cells were resuspended in 5 ml HBSS, 20mM HEPES, 0.5% BSA and incubated for 30 minutes at 37°C with 5 µl 5 mM dichloro-dihydrofluorescein diacetate (H<sub>2</sub>DCFDA, Molecular Probes, Eugene, Oregon).  $2 \times 10^5$  H<sub>2</sub>DCFDA-labeled cells were loaded in each well of a flat-bottomed 96 well plate. 10 µl of each agonist was added simultaneously into the well of the flat-bottomed plate to give final concentrations of  
25 100 ng/ml (fMLP was used at 10 µM). The plate was then read on a Victor<sup>2</sup> 1420 multilabel counter (Wallac, Turku, Finland) with a 485 nm excitation wavelength and 535 nm emission wavelength. Relative fluorescence was measured at 5 minute intervals over 60 minutes.

A pronounced respiratory burst was identified in PBMC with a 2.5 fold difference  
30 between control treated cells (TR1) and cells treated with 100 ng/ml muKS1 (Fig. 8).

Human stromal derived factor-1 $\alpha$  (SDF1 $\alpha$ ) (100 ng/ml) and 10  $\mu$ M formyl-Met-Leu-Phe (fMLP) were used as positive controls.

#### *Chemotaxis assay*

Cell migration in response to muKS1 was tested using a 48 well Boyden's chamber (Neuro Probe Inc., Cabin John, Maryland) as described in the manufacturer's protocol. In brief, agonists were diluted in HBSS, 20mM HEPES, 0.5% BSA and added to the bottom wells of the chemotactic chamber. THP-1 cells were re-suspended in the same buffer at  $3 \times 10^5$  cells per 50  $\mu$ l. Top and bottom wells were separated by a PVP-free polycarbonate filter with a 5  $\mu$ m pore size for monocytes or 3  $\mu$ m pore size for lymphocytes. Cells were added to the top well and the chamber incubated for 2 hours for monocytes and 4 hours for lymphocytes in a 5% CO<sub>2</sub> humidified incubator at 37°C. After incubation, the filter was fixed and cells scraped from the upper surface. The filter was then stained with Diff-Quick (Dade International Inc., Miami, Florida) and the number of migrating cells counted in five randomly selected high power fields. The results are expressed as a migration index (the number of test migrated cells divided by the number of control migrated cells).

Using this assay, muKS1 was tested against T cells and THP-1 cells. MuKS1 induced a titrateable chemotactic effect on THP-1 cells from 0.01 ng/ml to 100 ng/ml (Fig. 9). Human SDF1 $\alpha$  was used as a positive control and gave an equivalent migration. MuKS1 was also tested against IL-2 activated T cells. However, no migration was evidence for muKS1 even at high concentrations, whereas SDF-1 $\alpha$  provided an obvious titrateable chemotactic stimulus. Therefore, muKS1 appears to be chemotactic for THP-1 cells but not for IL-2 activated T cells at the concentrations tested.

#### *Full length sequence of muKS1 clone*

The nucleotide sequence of muKS1 was extended by determining the base sequence of additional ESTs. Combination of all the ESTs identified the full-length muKS1 (SEQ ID NO: 370) and the corresponding translated polypeptide sequence in SEQ ID NO: 394.

#### *Analysis of human RNA transcripts by Northern blotting*

Northern blot analysis to determine the size and distribution of mRNA for the human homologue of muKS1 was performed by probing human tissue blots (Clontech,

Palo Alto, California) with a radioactively labeled probe consisting of nucleotides 1 to 288 of huKS1 (SEQ ID NO: 270). Prehybridization, hybridization, washing, and probe labeling were performed as described in Sambrook, *et al.*, *Ibid.* mRNA for huKS1 was 1.6 kb in size and was observed to be most abundance in kidney, liver, colon, small intestine, and spleen. Expression could also be detected in pancreas, skeletal muscle, placenta, brain, heart, prostate, and thymus. No detectable signal was found in lung, ovary, and testis.

*Analysis of human RNA transcripts in tumor tissue by Northern blotting*

Northern blot analysis to determine distribution of huKS1 in cancer tissue was performed as described previously by probing tumor panel blots (Invitrogen, Carlsbad, California). These blots make a direct comparison between normal and tumor tissue. MRNA was observed in normal uterine and cervical tissue but not in the respective tumor tissue. In contrast, expression was up-regulated in breast tumor and down-regulated in normal breast tissue. No detectable signal was found in either ovary or ovarian tumors.

Injection of bacterially expressed muKS1a into nude mice

Two nude mice were anaesthetised intraperitoneally with 75 µl of 1/10 dilution of Hypnorm (Janssen Pharmaceuticals, Buckinghamshire, England) in phosphate buffered saline. 20ug of bacterially expressed muKS1a (SEQ ID NO: 345) was injected subcutaneously in the left hind foot, ear and left-hand side of the back. The same volume of phosphate buffered saline was injected in the same sites but on the right-hand side of the same animal. Mice were left for 18 hours and then examined for inflammation. Both mice showed a red swelling in the ear and foot sites injected with the bacterially expressed protein. No obvious inflammation could be identified in either back site. Mice were culled and biopsies taken from the ear, back and foot sites and fixed in 3.7% formol saline. Biopsies were embedded, sectioned and stained with Haemotoxylin and eosin. Sites injected with muKS1a had a marked increase in polymorphonuclear granulocytes, whereas sites injected with phosphate buffered saline had a low background infiltrate of polymorphonuclear granulocytes.

*Injection of bacterially recombinant muKS1 into C3H/HeJ mice*

Eighteen C3H/HeJ mice were divided into 3 groups and injected intraperitoneally with muKS1, GV14B, or phosphate buffered saline (PBS). GV14B is a bacterially

expressed recombinant protein used as a negative control. Group 1 mice were injected with 50 µg of muKS1 in 1 ml of PBS; Group 2 mice were injected with 50 µg of GV14B in 1 ml of PBS; and Group 3 mice with 1 ml of PBS. After 18 hours, the cells in the peritoneal cavity of the mice were isolated by intraperitoneal lavage with 2 x 4 ml washes with harvest solution (0.02% EDTA in PBS). Viable cells were counted from individual mice from each group. Mice injected with 50 µg of muKS1 had on average a 3-fold increase in cell numbers (Fig. 10).

20 µg of bacterial recombinant muKS1 was injected subcutaneously into the left hind foot of three C3H/HeJ mice. The same volume of PBS was injected into the same site on the right-hand side of the same animal. After 18 hours, mice were examined for inflammation. All mice showed a red swelling in the foot pad injected with bacterially recombinant KS1. From histology, sites injected with muKS1 had an inflammatory response of a mixed phenotype with mononuclear and polymorphonuclear cells present.

Chemokines are a large superfamily of highly basic secreted proteins with a broad number of functions (Baggiolini, *et al.*, *Annu. Rev. Immunol.*, 15:675-705, 1997; Ward, *et al.*, *Immunity*, 9:1-11, 1998; Horuk, *Nature*, 393:524-525, 1998). The polypeptide sequences of muKS1 and huKS1 have similarity to CXC chemokines, suggesting that this protein will act like other CXC chemokines. The *in vivo* data from nude mice supports this hypothesis. This chemokine-like protein may therefore be expected to stimulate leukocyte, epithelial, stromal, and neuronal cell migration; promote angiogenesis and vascular development; promote neuronal patterning, hemopoietic stem cell mobilization, keratinocyte and epithelial stem cell patterning and development, activation and proliferation of leukocytes; and promotion of migration in wound healing events. It has recently been shown that receptors to chemokines act as co-receptors for HIV-1 infection of CD4+ cells (Cairns, *et al.*, *Nature Medicine*, 4:563-568, 1998) and that high circulating levels of chemokines can render a degree of immunity to those exposed to the HIV virus (Zagury, *et al.*, *Proc. Natl. Acad. Sci. USA* 95:3857-3861, 1998). This novel gene and its encoded protein may thus be usefully employed as regulators of epithelial, lymphoid, myeloid, stromal, and neuronal cells migration and cancers; as agents for the treatment of cancers, neuro-degenerative diseases, inflammatory autoimmune diseases

such as psoriasis, asthma and Crohn's disease for use in wound healing; and as agents for the prevention of HIV-1 binding and infection of leukocytes.

We have also shown that muKS1 can promote a quantifiable increase in cell numbers in the peritoneal cavity of C3H/HeJ mice injected with muKS1. Furthermore, we have shown that muKS1 can induce an oxidative burst in human peripheral blood mononuclear cells and migration in the human monocyte leukemia cell line, THP-1, suggesting that monocyte/macrophages are one of the responsive cell types for KS1. In addition to this, we demonstrated that huKS1 was expressed at high levels in a number of non-lymphoid tissues, such as the colon and small intestine, and in breast tumors. It was also expressed in normal uterine and cervical tissue, but was completely down-regulated in their respective tumors. It has recently been shown that non-ELR chemokines have demonstrated angiostatic properties. IP-10 and Mig, two non-ELR chemokines, have previously been shown to be up-regulated during regression of tumors (Tannenbaum CS, Tubbs R, Armstrong D, Finke JH, Bukowski RM, Hamilton TA, "The CXC Chemokines IP-10 and Mig are necessary for IL-12-mediated regression of the mouse RENCA tumor," *J. Immunol.* 161: 927-932, 1998), with levels of expression inversely correlating with tumor size (Kanegane C, Sgadari C, Kanegane H, Teruya-Feldstine J, Yao O, Gupta G, Farber JM, Liao F, Liu L, Tosato G, "Contribution of the CXC Chemokines IP-10 and Mig to the antitumor effects of IL-12," *J. Leuko. Biol.* 64: 384-392, 1998). Furthermore, neutralizing antibodies to IP-10 and Mig would reduce the anti-tumor effect, indicating the contribution these molecules make to the anti-tumor effects. Therefore, it is expected that in the case of cervical and uterine tumors, KS1 would have similar properties.

The data demonstrates that KS1 is involved in cell migration showing that one of the responsive cell types is monocyte/macrophage. The human expression data in conjunction with the *in vitro* and *in vivo* biology demonstrates that this molecule may be a useful regulator in cell migration, and as an agent for the treatment of inflammatory diseases, such as Crohn's disease, ulcerative colitis, and rheumatoid arthritis; and cancers, such as cervical adenocarcinoma, uterine leiomyoma, and breast invasive ductal carcinoma.

### Example 6

#### CHARACTERIZATION OF KS2

KS2 contains a transmembrane domain and may function as either a membrane-bound ligand or a receptor. Northern analysis indicated that the mRNA for KS2 was expressed in the mouse keratinocyte cell line, Pam212, consistent with the cDNA being identified in mouse keratinocytes.

#### Mammalian Expression

To express KS2, the extracellular domain was fused to the amino terminus of the constant domain of immunoglobulinG (Fc) that had a C-terminal 6xHistidine tag. This was performed by cloning polynucleotides 20-664 of KS2 (SEQ ID NO: 273), encoding amino acids 1-215 of polypeptide KS2 (SEQ ID NO: 347), into the mammalian expression vector pcDNA3 (Invitrogen, NV Leek, Netherlands), to the amino terminus of the constant domain of immunoglobulinG (Fc) that had a C-terminal 6xHistidine tag. This construct was transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid.* The Fc fusion construct of KS2a was expressed by transfecting Cos-1 cells in 5 x T175 flasks with 180 µg of KS1a using DEAE-dextran. The supernatant was harvested after seven days and passed over a Ni-NTA column. Bound KS2a was eluted from the column and dialysed against PBS.

The ability of the Fc fusion polypeptide of KS2a to inhibit the IL-2 induced growth of concanavalin A stimulated murine splenocytes was determined as follows. A single cell suspension was prepared from the spleens of BALB/c mice and washed into DMEM (GIBCO-BRL) supplemented with 2 mM L-glutamine, 1 mM sodium pyruvate, 0.77 mM L-asparagine, 0.2 mM L-arginine, 160 mM penicillin G, 70 mM dihydrostreptomycin sulfate,  $5 \times 10^{-2}$  mM beta mercaptoethanol and 5% FCS (cDMEM). Splenocytes ( $4 \times 10^6$ /ml) were stimulated with 2 µg/ml concanavalin A for 24 hrs at 37°C in 10% CO<sub>2</sub>. The cells were harvested from the culture, washed 3 times in cDMEM and resuspended in cDMEM supplemented with 10 ng/ml rhuIL-2 at  $1 \times 10^5$  cells/ml. The assay was performed in 96 well round bottomed plates in 0.2 ml cDMEM. The Fc fusion polypeptide of KS2a, PBS, LPS and BSA were titrated into the plates and  $1 \times 10^4$  activated T cells (0.1 ml) were added to each well. The plates were incubated for 2 days in an atmosphere containing 10% CO<sub>2</sub> at 37°C. The degree of proliferation was

determined by pulsing the cells with 0.25 uCi/ml tritiated thymidine for the final 4 hrs of culture after which the cells were harvested onto glass fiber filtermats and the degree of thymidine incorporation determined by standard liquid scintillation techniques. As shown in Fig. 6, the Fc fusion polypeptide of KS2a was found to inhibit the IL-2 induced growth of concanavalin A stimulated murine splenocytes, whereas the negative controls PBS, BSA and LPS did not.

This data demonstrates that KS2 is expressed in skin keratinocytes and inhibits the growth of cytokine induced splenocytes. This suggests a role for KS2 in the regulation of skin inflammation and malignancy.

#### Example 7

##### Characterization of KS3

KS3 encodes a polypeptide of 40 amino acids (SEQ ID NO: 129). KS3 contains a signal sequence of 23 amino acids that would result in a mature polypeptide of 17 amino acids (SEQ ID NO: 348; referred to as KS3a).

KS3a was prepared synthetically (Chiron Technologies, Victoria, Australia) and observed to enhance transferrin-induced growth of the rat intestinal epithelial cells IEC-18 cells. The assay was performed in 96 well flat-bottomed plates in 0.1 ml DMEM (GIBCO-BRL Life Technologies) supplemented with 0.2% FCS. KS3a (SEQ ID NO: 348), apo-Transferrin, media and PBS-BSA were titrated either alone, with 750 ng/ml Apo-transferrin or with 750 ng/ml BSA, into the plates and  $1 \times 10^3$  IEC-18 cells were added to each well. The plates were incubated for 5 days at 37°C in an atmosphere containing 10% CO<sub>2</sub>. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 7, KS3a plus Apo-transferrin was found to enhance transferrin-induced growth of IEC-18 cells, whereas KS3a alone or PBS-BSA did not, indicating that KS3a and Apo-transferrin act synergistically to induce the growth of IEC-18 cells.

This data indicates that KS3 is epithelial derived and stimulates the growth of epithelial cells of the intestine. This suggests a role for KS3 in wound healing, protection from radiation- or drug-induced intestinal disease, and integrity of the epithelium of the intestine.

SEQ ID NOS: 1-409 are set out in the attached Sequence Listing. The codes for polynucleotide and polypeptide sequences used in the attached Sequence Listing confirm to WIPO Standard ST.25 (1988), Appendix 2.

5 All references cited herein, including patent references and non-patent references, are hereby incorporated by reference in their entireties.

Although the present invention has been described in terms of specific embodiments, changes and modifications can be carried out without departing from the scope of the invention which is intended to be limited only by the scope of the appended claims.

10



We claim:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of: (1) the sequences recited in SEQ ID NO: 1-119, 198-274,  
5 349-372, and 399-405; (2) complements of the sequences recited in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405; (3) reverse complements of the sequences recited in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405; (4) reverse sequences of the sequences recited in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405; (5) sequences having at least a 99% probability of being the same as a sequence selected from any of  
10 the sequences in (1)-(4), above, as measured by the computer algorithm BLASTP using the running parameters described above; and (6) nucleotide sequences having at least 50% identity to any of the sequences in (1)-(4), above, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.
- 15 2. An expression vector comprising an isolated polynucleotide of claim 1.
3. A host cell transformed with an expression vector of claim 2.
4. An isolated polypeptide comprising an amino acid sequence selected from  
20 the group consisting of: (1) sequences provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409; (2) sequences having at least a 99% probability of being the same as a sequence of SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, as measured by the computer algorithm BLASTP using the running parameters described above; and (3) sequences having at least 50% identity to a sequence provided in SEQ ID NO:  
25 120-197, 275-348, 373-398, and 406-409, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.
5. An isolated polynucleotide encoding a polypeptide of claim 4.
- 30 6. An expression vector comprising an isolated polynucleotide of claim 5.

7. A host cell transformed with an expression vector of claim 6.

8. An isolated polypeptide comprising at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of:  
5 (1) sequences provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409;  
(2) sequences having at least a 99% probability of being the same as a sequence of SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, as measured by the computer algorithm BLASTP using the running parameters described above; and (3) sequences  
10 having at least 50% identity to a sequence provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

9. A method for stimulating keratinocyte growth and motility in a patient, comprising administering to the patient a composition comprising an isolated  
15 polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

10. The method of claim 9, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 342, 343, 397 and 398; (2) sequences having at least about 50% identity to a  
20 sequence of SEQ ID NO: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

11. A method for inhibiting the growth of cancer cells in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the  
25 polypeptide comprising an amino acid sequence of claim 4.

12. The method of claim 11, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 342, 343, 397 and 398; and (2) sequences having at least 50% identity to a  
30 sequence of SEQ ID NO: 187, 196, 342, 343, 397, and 398, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

13. A method for modulating angiogenesis in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

5

14. A method of claim 13, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 342, 343, 397 and 398; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 187, 196, 342, 343, 397 and 398 as measured by the computer  
10 algorithm BLASTP, using the running parameters and identity test defined above.

15. A method for inhibiting angiogenesis and vascularization of tumors in a patient, comprising administering to a patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

15

16. The method of claim 15, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 342, 343, 397, and 398; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 187, 196, 340, 342-346, 397, and 398, as measured by the  
20 computer algorithm BLASTP, using the running parameters and identity test defined above.

17. A method for modulating skin inflammation in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the  
25 polypeptide comprising an amino acid sequence of claim 4.

18. The method of claim 17, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 338 and 347; and (2) sequences having at least 50% identity to a sequence of SEQ ID  
30 NO: 338 and 347 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

19. A method for stimulating the growth of epithelial cells in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

5

20. The method of claim 19, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 129 and 348; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 129 and 348 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

10

21. A method for inhibiting the binding of HIV-1 to leukocytes in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

15

22. A method of claim 21, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 340, 344, 345 and 346; (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 340, 344, 345 and 346 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

20

23. A method for treating an inflammatory disease in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

25

24. The method of claim 23, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 340, 344, 345 and 346; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 340, 344, 345 and 346 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

30

25. A method for treating cancer in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

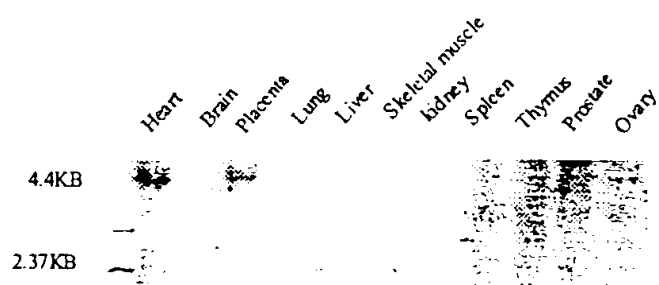
5           26. The method of claim 25, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 340, 344, 345 and 346; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 340, 344, 345 and 346 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

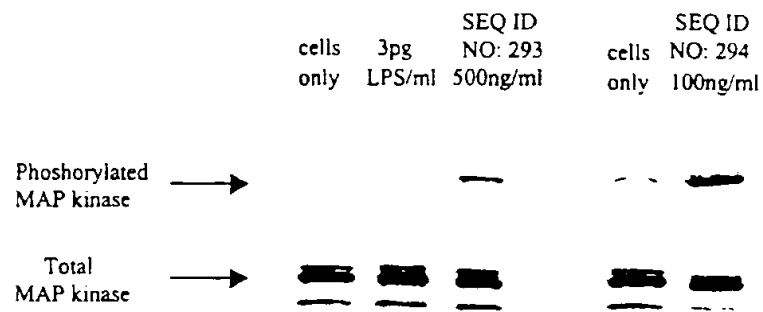
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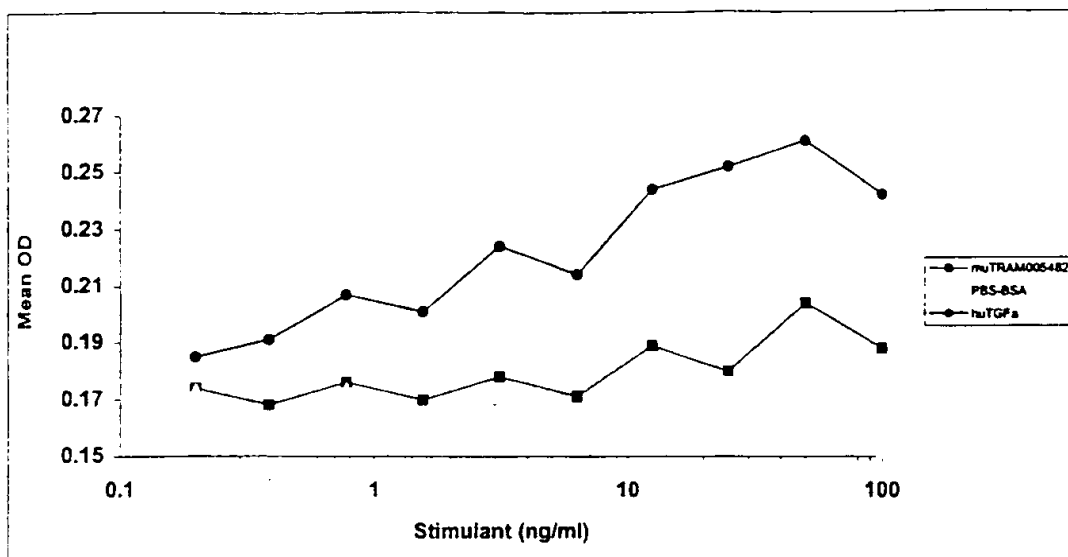
27. A method for treating neurological disease in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

15           28. The method of claim 27, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 340, 342-346, and 395; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 187, 196, 340, 342-346, and 395, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

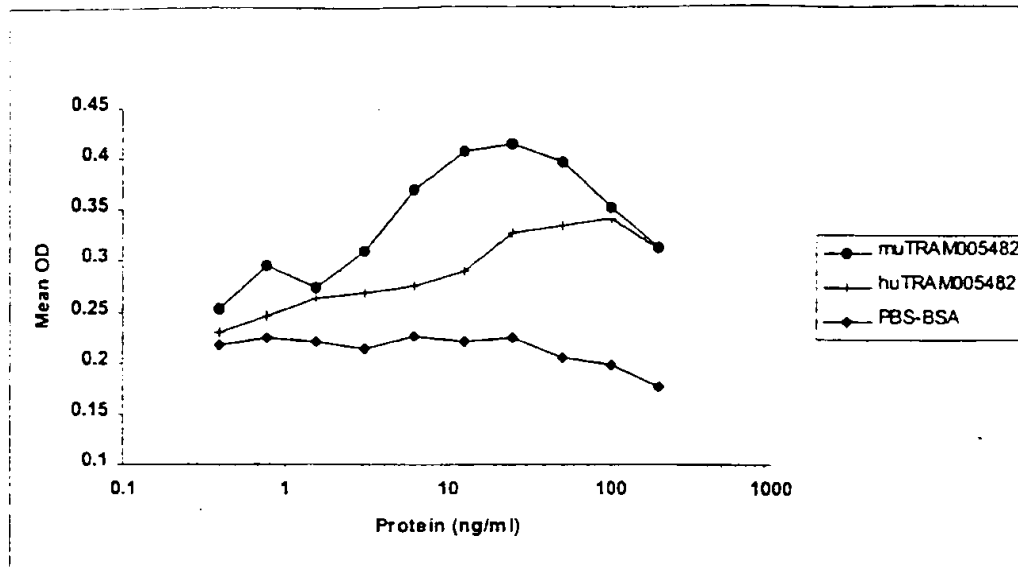
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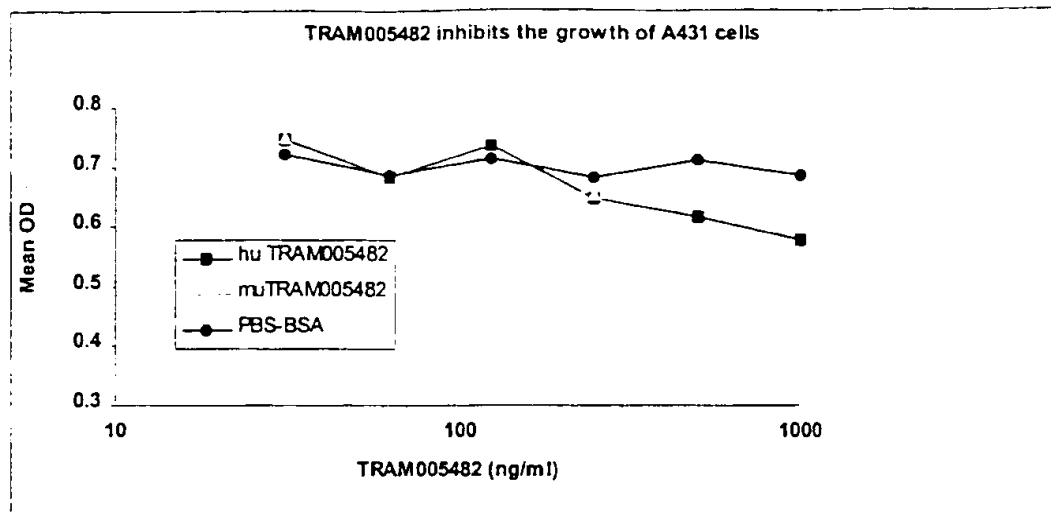
1/14  
Figure 1Distribution of human TAK1 mRNA in human tissues

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Figure 2

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Figure 3



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Figure 4

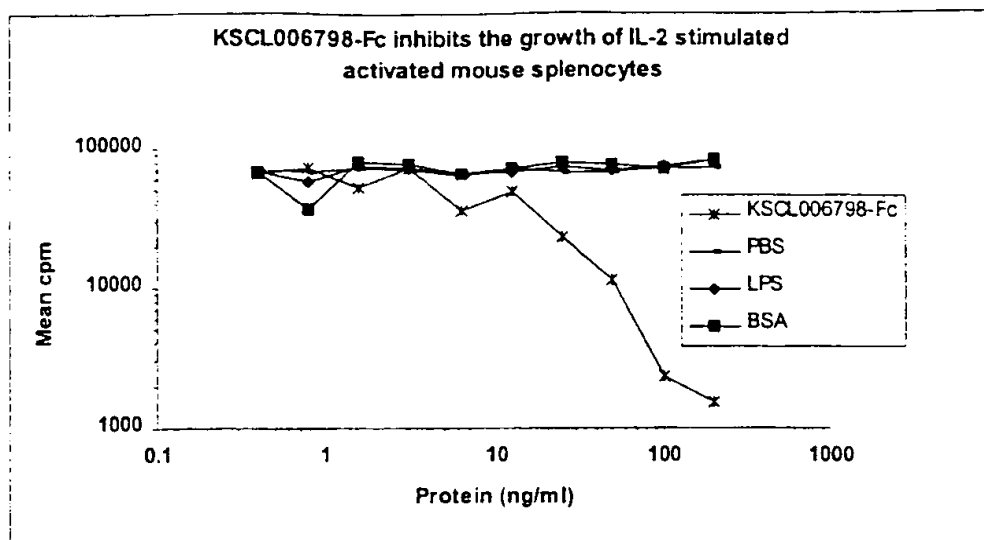
5/14  
Figure 5

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Figure 6

Key: Br, Brain; Th, Thymus; Sk, Skin; Ht, Heart; Lg, Lung; Spl, Spleen; Sth, Stomach; Kdy, Kidney; Lr, Liver; LI, Lower intestine; Ts, Testis; Mle, Muscle.

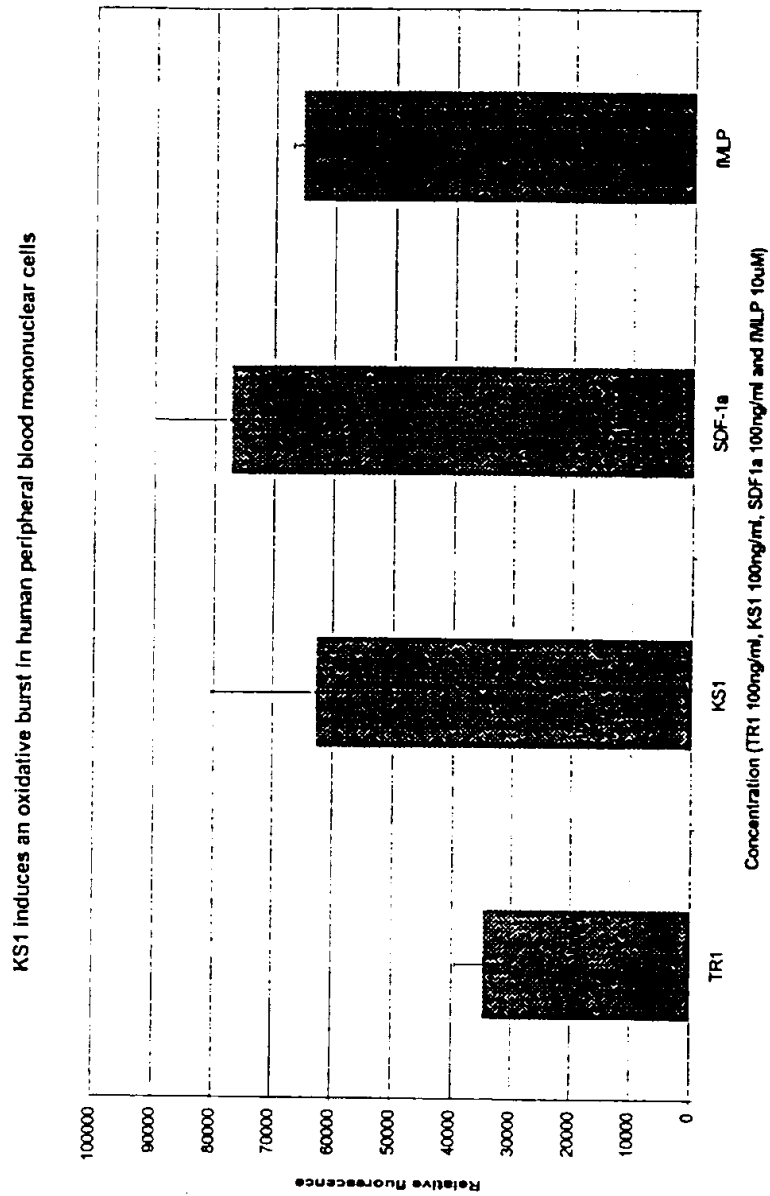
Br Th      Sk Ht Lg Spl Sth Kdy Lr LI Mle



7/14  
Figure 7

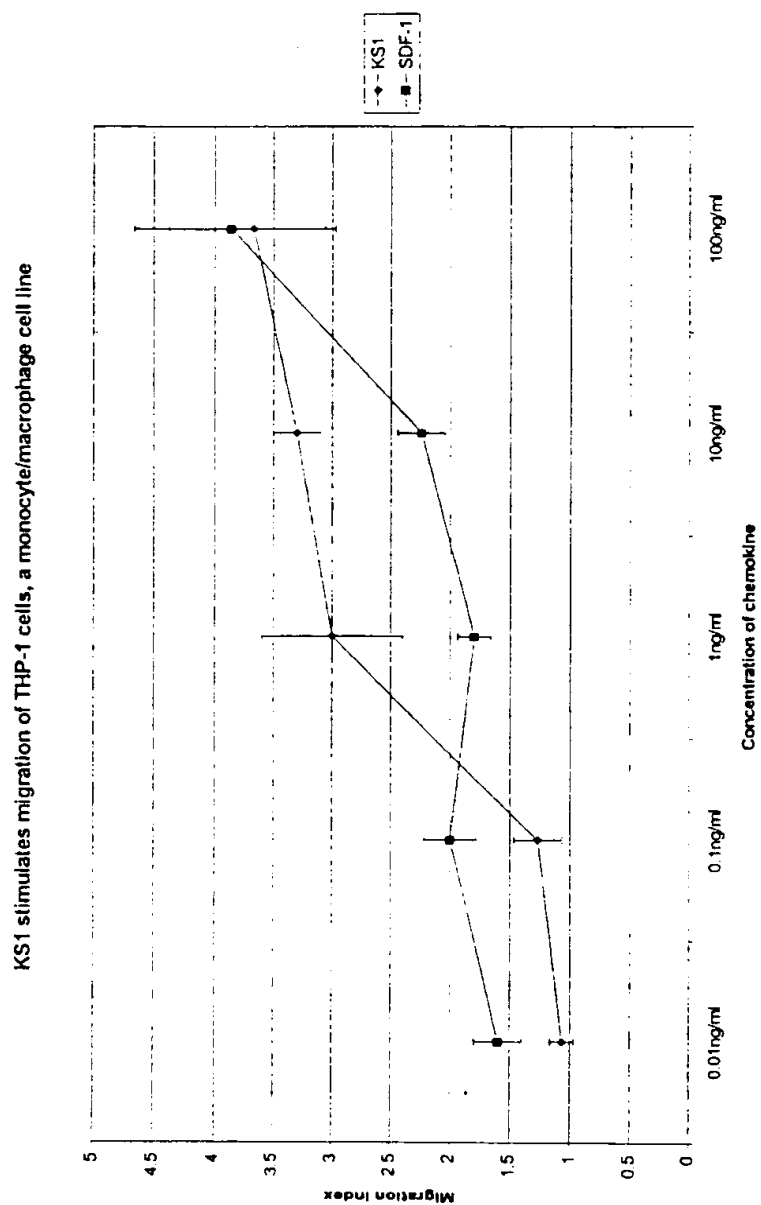
8/14

Figure 8



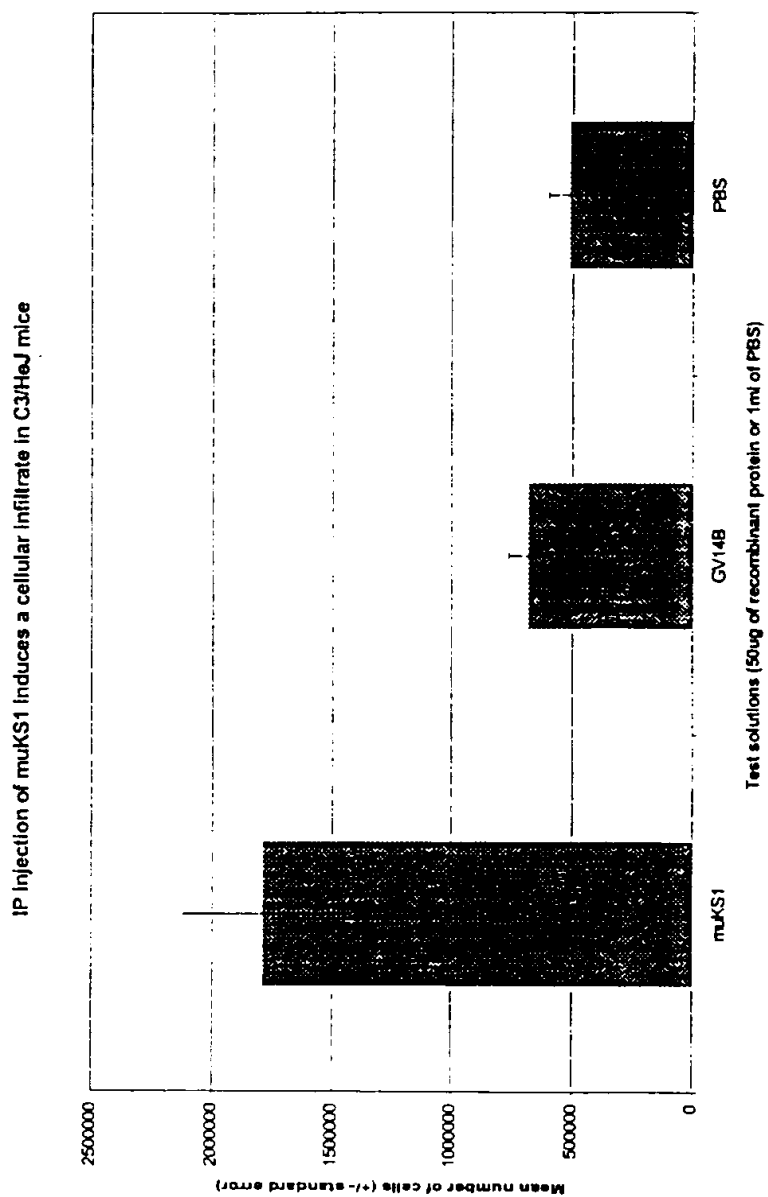
9/14

Figure 9



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Figure 10



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Figure 11

Cell Line	Cells stimulated with		
	PBS	Hu TR1	
CV1/EBNA		— ←	ERK1/2
HeLa		— ←	ERK1/2



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Figure 12

mu and huTR1 upregulate huTR1 mRNA expression in HeLa cells

HeLa cells stimulated with

PBS muTR1 huTR1 huTGF $\alpha$



huTR1 mRNA

Actin mRNA

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Figure 13A

Murine Tr1 activates the SRE reporter in PC12SRE cells

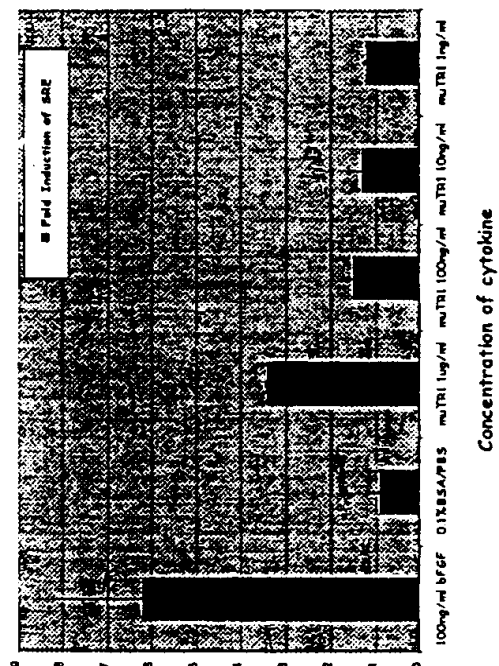
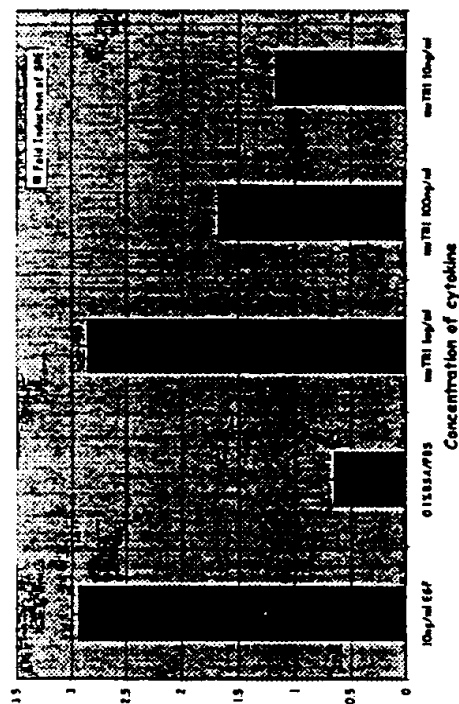


Figure 13B

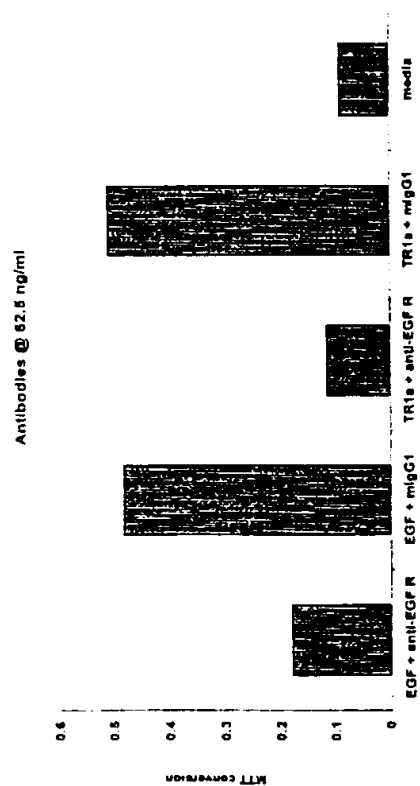
Murine Tr1 activates the SRE reporter in HecatsSRE cells



14/14

Figure 14

TR1 growth of HaCat cells is inhibited by an antibody to the EGF receptor



## SEQUENCE LISTING

&lt;110&gt;

Watson, James D.  
 Strachan, Lorna  
 Sleeman, Matthew  
 Onrust, Rene  
 Murison, James Greg  
 Kumble, Anand

<120> Compositions isolated from skin cells  
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 <212> DNA  
 <213> mouse

<400> 13						
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 <212> DNA  
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<210> 15  
 <211> 318  
 <212> DNA  
 <213> Rat

<400> 15						
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 <211> 856  
 <212> DNA  
 <213> Rat

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 <212> DNA  
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<400> 17						
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 <213> Rat

<220>						
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&lt;210&gt; 19

&lt;211&gt; 750

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 19

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&lt;210&gt; 20

&lt;211&gt; 849

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 20

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&lt;211&gt; 312

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 21

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312

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 <212> DNA  
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 <212> DNA  
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<400> 24  
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&lt;210&gt; 25

&lt;211&gt; 1230

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 25

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&lt;210&gt; 26

&lt;211&gt; 393

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 26

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&lt;210&gt; 27

&lt;211&gt; 778

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 27

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&lt;210&gt; 28

&lt;211&gt; 1123

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 28

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&lt;210&gt; 29

&lt;211&gt; 849

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 29

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gaccagcc						849

&lt;210&gt; 30

&lt;211&gt; 1015

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;220&gt;

&lt;400&gt; 30

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&lt;210&gt; 31

&lt;211&gt; 452

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 31

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&lt;210&gt; 32

&lt;211&gt; 434

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 32

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gaaagagcgt	cgcc					434

&lt;210&gt; 33

&lt;211&gt; 903

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 33

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cct						903

&lt;210&gt; 34

&lt;211&gt; 1359

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (644)... (644)

&lt;400&gt; 34

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&lt;210&gt; 35

&lt;211&gt; 797

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 35

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 <212> DNA  
 <213> mouse

<400> 36						
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<210> 37  
 <211> 501  
 <212> DNA  
 <213> mouse

<400> 37						
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<210> 38  
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 <212> DNA  
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<400> 38						
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766

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<212> DNA  
<213> mouse

<400> 39  
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<210> 40  
<211> 962  
<212> DNA  
<213> mouse

<400> 40  
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<211> 794  
<212> DNA  
<213> mouse

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<210> 42  
 <211> 1152  
 <212> DNA  
 <213> mouse

<400> 42  
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 gcctgcccag cc 1152

<210> 43  
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 <212> DNA  
 <213> mouse

<400> 43  
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 aacaagaact agggccagca agtggcttaa ggggtgcctgc taaccatctc agccacctga 420  
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<210> 44  
 <211> 391  
 <212> DNA  
 <213> mouse

<400> 44  
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 gagatggggc tccctgggagc tcaggcgatg agccccatc gtctcctcc caagacgagg 300  
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 <212> DNA  
 <213> Rat

<400> 45  
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 <212> DNA  
 <213> mouse

<400> 46  
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 <212> DNA  
 <213> mouse

<400> 47  
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<210> 48  
 <211> 159  
 <212> DNA  
 <213> mouse

<220>  
 <221> unsure  
 <222> (3)... (3)

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<210> 49  
 <211> 465  
 <212> DNA  
 <213> Rat

<400> 49  
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&lt;210&gt; 50

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;220&gt;

&lt;400&gt; 50

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&lt;210&gt; 51

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (80)...(80)

&lt;221&gt; unsure

&lt;222&gt; (312)...(312)

&lt;221&gt; unsure

&lt;222&gt; (319)...(319)

&lt;221&gt; unsure

&lt;222&gt; (353)...(354)

&lt;400&gt; 51

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&lt;210&gt; 52

&lt;211&gt; 228

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 52

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gagagtcac	actgacaaca	gagatggacc	agtacagaat	tacctgct		228

<210> 53  
 <211> 361  
 <212> DNA  
 <213> Human

<400> 53  
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<210> 54  
 <211> 403  
 <212> DNA  
 <213> Human

<220>

<400> 54  
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<210> 55  
 <211> 413  
 <212> DNA  
 <213> Human

<400> 55  
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<210> 56  
 <211> 452  
 <212> DNA  
 <213> Human

<400> 56  
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<210> 57

&lt;211&gt; 190

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;220&gt;

&lt;400&gt; 57

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cagtgtgcaa	catatataaa	acagaaatac	taactctaca	ggcagtatgt	cgacgcggcc	180
gcgtattcgg						190

&lt;210&gt; 58

&lt;211&gt; 413

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 58

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&lt;210&gt; 59

&lt;211&gt; 325

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (213) ... (213)

&lt;221&gt; unsure

&lt;222&gt; (223) ... (223)

&lt;221&gt; unsure

&lt;222&gt; (227) ... (227)

&lt;221&gt; unsure

&lt;222&gt; (243) ... (243)

&lt;400&gt; 59

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&lt;210&gt; 60

&lt;211&gt; 372

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 60

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&lt;210&gt; 61

&lt;211&gt; 363

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (15)...(15)

&lt;400&gt; 61

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aggagagcat	cgtgggtgat	ggcgagacaa	aggagccctt	ttactggtgc	agtactctgc	360
ttaa						363

&lt;210&gt; 62

&lt;211&gt; 399

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 62

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ggtctttttt	tttcttcttc	tttttctttt	gctcccaaa			399

&lt;210&gt; 63

&lt;211&gt; 399

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;400&gt; 63

caaagcccac	tgtaggctcc	gctgaggtag	cgattgctgt	atttctggtc	atctgcatca	60
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tcttcttacc	tctttcctgg	gcatacttac	gctgtctcag	aagacagatc	tctgggcctc	360
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&lt;210&gt; 64

&lt;211&gt; 2481

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 64

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ctgcatttgg	aaaaaaaaa	a				2481

&lt;210&gt; 65

&lt;211&gt; 3008

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;400&gt; 65

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aaaaaaaa						3008

&lt;210&gt; 66

&lt;211&gt; 1888

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (1690)... (1690)

&lt;221&gt; unsure

&lt;222&gt; (1755)... (1755)

&lt;221&gt; unsure

&lt;222&gt; (1864)... (1864)

&lt;400&gt; 66

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accngtggct	cgcatttctca	ttgacctg				1888

&lt;210&gt; 67

&lt;211&gt; 1260

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 67

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&lt;210&gt; 68

&lt;211&gt; 1729

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 68

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&lt;210&gt; 69

&lt;211&gt; 355

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 69

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&lt;210&gt; 70

&lt;211&gt; 1421

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 70

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&lt;210&gt; 71

&lt;211&gt; 378

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 71

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&lt;210&gt; 72

&lt;211&gt; 267

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 72

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&lt;210&gt; 73

&lt;211&gt; 1633

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;400&gt; 73

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&lt;210&gt; 74

&lt;211&gt; 1252

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 74

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&lt;210&gt; 75

&lt;211&gt; 2411

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 75

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&lt;210&gt; 76

&lt;211&gt; 1335

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 76

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<400> 88  
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 gtctcctgag acgctgagaa acccttcctt gcagctataa tgggcctggc cgcccagtg 240  
 ggagctgtag ctccccacga cgtagccctc aggaacttca ggagggatgc cacagtctat 300  
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 catctctctg caccataacc ccattgctca cccccagac cctgtgttag 410

<210> 89  
 <211> 279  
 <212> DNA  
 <213> mouse

<220>

<400> 89  
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 agaagagttt atgggaaatc ttggagaaaa cattggatgg tttagagaa tggtaggag 180  
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 gacagggtgg agggcattgt ccgacagaac cattgctgt 279

<210> 90  
 <211> 398  
 <212> DNA  
 <213> mouse

<400> 90  
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actcttagac	atgggtgtgc	tactgaact	ctagggctctg	tgtgctagat	gctgccaacg	180
ctgtattcag	gacctgaagt	gagtaccctg	gtggatccag	accaatccag	tgtgagacta	240
ctgaagaaca	tctgttgcca	gaacggccac	accaaacaga	tggagtgcc	cagcacttag	300
cttcttaaat	aacatcgga	ccattcagcc	agcgagtctg	tgtttgcttt	ttgttaaatt	360
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 <211> 279  
 <212> DNA  
 <213> mouse

<400> 91						
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gttcgaggaa	gcccggctgg	accatagtgg	ccacggcggt	gaggtaggcg	tggacagggc	180
tgaccagtc	aagttaagga	cgttcgggtc	catgttaacc	ctgccttgta	cgtccagcat	240
cgtaagaaaa	aacacttgag	aaccgaaga	ggagatgga			279

<210> 92  
 <211> 401  
 <212> DNA  
 <213> mouse

<400> 92						
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tccatagatg	ggcagatggg	tcccaaagtt	acactacaga	actacaaatc	gactcttaaa	240
attaaaacgg	gactttacaa	gcattctaga	agactcaaac	ttgaagcaat	ttttggaaaa	300
taaagtgtaca	gagaaaagat	cttgaagcta	ctgaacagag	aacctcatt	aaccgagcaa	360
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<210> 93  
 <211> 339  
 <212> DNA  
 <213> mouse

<400> 93						
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catgatgcag	cctggccttt	cctagagcct	gtgaaccctc	gcttggtgag	tggataaccga	240
cgtgtcatca	agaaccttat	ggatttttcc	accatgcgag	aacgcctgct	ccgtggagggg	300
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<210> 94  
 <211> 55  
 <212> DNA  
 <213> mouse

<400> 94						
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<210> 95  
 <211> 186  
 <212> DNA  
 <213> mouse

<400> 95						
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gcggggcccc	agaaacaaga	agcgcggctg	gaggaggctc	gccgaggagc	cgctgggggtt	120

agaggtcgac cagttcctgg aagacgtccg gctacaggag cgcacgaccg gtggcttgtt 180  
ggcaga 186

<210> 96  
<211> 244  
<212> DNA  
<213> mouse

<400> 96  
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aagagggcat gaggcacacc ctgatcactg tctcaggcct ttgtgggcac tgactcgacc 180  
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cctt 244

<210> 97  
<211> 116  
<212> DNA  
<213> mouse

<220>  
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<222> (11) ... (11)

<221> unsure  
<222> (13) ... (13)

<221> unsure  
<222> (41) ... (41)

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<211> 307  
<212> DNA  
<213> mouse

<400> 98  
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tgagcaattt cgggatatgc cctaccagcc attcagcaaa ggagatcggc tgggaaagg 180  
tgagactgg acagggggcca cataccagga caagaggtag acaaacaagt attcctctca 240  
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tgggtgg 307

<210> 99  
<211> 360  
<212> DNA  
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<220>

<400> 99  
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ccaggttgct cagaagcaca aagggtgtgg ctactggccc taaccatgga ctacgtggt 240  
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ctcggctt cctggcccat atggatgggc ttggcaagga acctacctct tctctaaggt 360

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<211> 257  
<212> DNA  
<213> mouse

<400> 100  
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gacgcatttc tatcgggt 257

<210> 101  
<211> 203  
<212> DNA  
<213> mouse

<400> 101  
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gcatactcaa gagggccacc agcaacgggtg tggtcagcag ccccaactcc accagcaggc 120  
cagcccttcc tgtcaagtcc ctagcacagc gggaggcaga gtatgcagag gctcggagac 180  
ggatcctagg cagtgccagc cct 203

<210> 102  
<211> 300  
<212> DNA  
<213> mouse

<400> 102  
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ggagcaagaa tgagcttagg ttgggaggga atggggcggtg ggggagctgg agcaagacca 180  
cggcctgggtg gcagccggtc gccctacagg cccattccc gcctggcact gtctcctta 240  
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<211> 370  
<212> DNA  
<213> mouse

<220>

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gttgaagctg ctggggaccg cacagaggag ttccacggcc acacggtgaa tctcctgggg 300  
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gagtcaatgg 370

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<211> 423  
<212> DNA  
<213> mouse

<400> 104  
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gagatccgca	aggaaatgat	gaaggagacc	ttcaagtact	tctccgaggt	accgatacgt	420
gat						423

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 <211> 117  
 <212> DNA  
 <213> mouse

<400> 105						
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gccccgcgtc	gtgactgggg	tctcacacag	gttcagcact	tgagcatag	tgaggtg	117

<210> 106  
 <211> 133  
 <212> DNA  
 <213> mouse

<400> 106						
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<210> 107  
 <211> 217  
 <212> DNA  
 <213> mouse

<220>  
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<221> unsure  
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<221> unsure  
 <222> (18) ... (23)

<221> unsure  
 <222> (34) ... (34)

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 <222> (37) ... (38)

<221> unsure  
 <222> (40) ... (42)

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 <222> (50) ... (52)

<221> unsure  
 <222> (55) ... (58)

<221> unsure  
 <222> (152) ... (152)

<221> unsure

&lt;222&gt; (155)...(155)

&lt;221&gt; unsure

&lt;222&gt; (165)...(165)

&lt;400&gt; 107

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gccccctctg	tctactccaa	catcaccctt	taccaga			217

&lt;210&gt; 108

&lt;211&gt; 346

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;400&gt; 108

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&lt;210&gt; 109

&lt;211&gt; 242

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 109

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gacccgaact	tccactgagt	acttcctgga	agcctgttct	cgagaggaga	gagactcctg	240
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&lt;210&gt; 110

&lt;211&gt; 310

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;220&gt;

&lt;400&gt; 110

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ggctgacccg						310

&lt;210&gt; 111

&lt;211&gt; 228

&lt;212&gt; DNA

&lt;213&gt; mouse

&lt;400&gt; 111

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gccctcaacc	ccccaaactc	tttggtatga	agtactttta	acattttatat	ttcattgtta	120

cacttttaaat	tttghtaagga	aaactctgat	atttcattcc	tcttgaacca	ctaattgtag	180
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<210> 112  
 <211> 292  
 <212> DNA  
 <213> mouse

<400> 112						
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<210> 113  
 <211> 255  
 <212> DNA  
 <213> mouse

<220>

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 <212> DNA  
 <213> mouse

<400> 114						
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tgccaaggag	gttttattcc	ttttttttt	aaagatgaca	aatgtacaga	tgtagtagta	180
gatgttaatg	tacagat					197

<210> 115  
 <211> 205  
 <212> DNA  
 <213> mouse

<400> 115						
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<210> 116  
 <211> 202  
 <212> DNA  
 <213> mouse

<220>

<400> 116						
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cacacacaca	ctgtccatcc	atagttactt	atcttagttt	ccattccctag	agagatctaa	180
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<210> 117  
 <211> 240  
 <212> DNA  
 <213> mouse

<400> 117						
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<210> 118  
 <211> 527  
 <212> DNA  
 <213> Human

<400> 118						
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 <211> 655  
 <212> DNA  
 <213> Rat

<400> 119						
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<210> 120  
 <211> 176  
 <212> PRT  
 <213> Rat

<400> 120														
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1				5				10					15	
Pro	Val	Val	Ala	Tyr	Ser	Val	Ser	Leu	Pro	Ala	Ser	Phe	Leu	Glu
			20					25					30	
Val	Ala	Gly	Ser	Gly	Glu	Ala	Glu	Gly	Ser	Ser	Ala	Ser	Ser	Pro
		35					40					45		



Leu Leu Pro Pro Arg Thr Pro Ala Phe Ser Pro Thr Pro Gly Arg Thr  
 50 55 60  
 Gln Pro Thr Ala Pro Val Gly Pro Val Pro Pro Thr Asn Leu Leu Asp  
 65 70 75 80  
 Gly Ile Val Asp Phe Phe Arg Gln Tyr Val Met Leu Ile Ala Val Val  
 85 90 95  
 Gly Ser Leu Thr Phe Leu Ile Met Phe Ile Val Cys Ala Ala Leu Ile  
 100 105 110  
 Thr Arg Gln Lys His Lys Ala Thr Ala Tyr Tyr Pro Ser Ser Phe Pro  
 115 120 125  
 Glu Lys Lys Tyr Val Asp Gln Arg Asp Arg Ala Gly Gly Pro His Ala  
 130 135 140  
 Phe Ser Glu Val Pro Asp Arg Ala Pro Asp Ser Arg Gln Glu Glu Gly  
 145 150 155 160  
 Leu Asp Phe Phe Gln Gln Leu Gln Ala Asp Ile Leu Ala Cys Tyr Ser  
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<210> 121  
 <211> 116  
 <212> PRT  
 <213> Rat

<400> 121  
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 20 25 30  
 Gln Ile Arg Asp Lys Ala Leu Phe His Asp Ser Ser Val Ile Pro Asp  
 35 40 45  
 Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr Pro Arg Arg Tyr  
 50 55 60  
 Phe Phe Met Val Glu Glu Asp Asn Thr Pro Leu Ser Val Thr Val Thr  
 65 70 75 80  
 Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu Ser Leu Gln Glu Leu Pro  
 85 90 95  
 Glu Glu Ser Ser Ala Asp Gly Ser Gly Asp Pro Glu Pro Leu Asp Gln  
 100 105 110  
 Gln Lys Gln Gln  
 115

<210> 122  
 <211> 64  
 <212> PRT  
 <213> Human

<400> 122  
 Met Asn Leu Leu Ile Gly Ser Ile Ile Leu Ser Ser Phe Leu Val Leu  
 1 5 10 15  
 Ser Asp Gly Asp Thr Thr Ala Ser Pro Ser Ser Met Ser Ser Ser  
 20 25 30  
 Val Leu Asn His Ile Ser Ser Ser Ser Ser Val Trp His Leu Phe  
 35 40 45  
 Asp Ile Cys Asp Ser Ser Lys Trp Asn Ala Tyr Cys Gln Val Trp Gly  
 50 55 60

<210> 123  
 <211> 68  
 <212> PRT  
 <213> Human

<400> 123

Met Leu Thr Leu Pro Ile Leu Val Cys Lys Val Gln Asp Ser Asn Arg  
 1 5 10 15  
 Arg Lys Met Leu Pro Thr Gln Phe Leu Phe Leu Leu Gly Val Leu Gly  
 20 25 30  
 Ile Phe Gly Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp Gly Ser Thr  
 35 40 45  
 Gly Pro Thr Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe  
 50 55 60  
 Ser Cys Leu Leu  
 65

<210> 124  
 <211> 110  
 <212> PRT  
 <213> mouse

<400> 124  
 Met Ile Ser Pro Ala Trp Ser Leu Phe Leu Ile Gly Thr Lys Ile Gly  
 1 5 10 15  
 Leu Phe Phe Gln Val Ala Pro Leu Ser Val Val Ala Lys Ser Cys Pro  
 20 25 30  
 Ser Val Cys Arg Cys Asp Ala Gly Phe Ile Tyr Cys Asn Asp Arg Ser  
 35 40 45  
 Leu Thr Ser Ile Pro Val Gly Ile Pro Glu Asp Ala Thr Thr Leu Tyr  
 50 55 60  
 Leu Gln Asn Asn Gln Ile Asn Asn Val Gly Ile Pro Ser Asp Leu Lys  
 65 70 75 80  
 Asn Leu Leu Lys Val Gln Arg Ile Tyr Leu Tyr His Asn Ser Leu Asp  
 85 90 95  
 Glu Phe Pro Thr Asn Leu Pro Lys Tyr Val Lys Glu Leu His  
 100 105 110

<210> 125  
 <211> 330  
 <212> PRT  
 <213> mouse

<400> 125  
 Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Leu Ser Leu Pro Leu Leu  
 1 5 10 15  
 Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala Cys Pro Cys Leu Arg  
 20 25 30  
 Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe  
 35 40 45  
 Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys  
 50 55 60  
 Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser  
 65 70 75 80  
 Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His  
 85 90 95  
 Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr  
 100 105 110  
 Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu  
 115 120 125  
 Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu  
 130 135 140  
 Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala  
 145 150 155 160  
 Ser Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser  
 165 170 175  
 Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly Gly His Thr Val Asp

180 185 190  
 Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys Ile Glu Ala Ser Tyr  
 195 200 205  
 Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser Trp  
 210 215 220  
 Pro Glu Ala Tyr Gly Ser Asp Phe Trp Gln Ser Ile Arg Phe Thr Asp  
 225 230 235 240  
 Tyr Ser Gln His Asn Gln Met Val Met Ala Leu Thr Leu Arg Cys Pro  
 245 250 255  
 Leu Lys Leu Glu Ala Ser Leu Cys Trp Arg Gln Asp Pro Leu Thr Pro  
 260 265 270  
 Cys Glu Thr Leu Pro Asn Ala Thr Ala Gln Glu Ser Glu Gly Trp Tyr  
 275 280 285  
 Ile Leu Glu Asn Val Asp Leu His Pro Gln Leu Cys Phe Lys Phe Ser  
 290 295 300  
 Phe Glu Asn Ser Ser His Val Glu Cys Pro His Gln Ser Gly Ser Leu  
 305 310 315 320  
 Pro Ser Trp Thr Val Ser Met Asp Thr Gln  
 325 330

&lt;210&gt; 126

&lt;211&gt; 37

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 126

Met Leu Trp Val Leu Leu Ser Leu Thr Pro Leu Leu Ser Pro Leu Ile  
 1 5 10 15  
 Phe Phe Pro Val Lys Thr Val Ala Leu Glu Glu Ile Ser Thr Ile Cys  
 20 25 30  
 Arg Ala Asp Val Leu  
 35

&lt;210&gt; 127

&lt;211&gt; 42

&lt;212&gt; PRT

&lt;213&gt; mouse

&lt;400&gt; 127

Met Gly Ser Pro Ile Ser Gly Val Cys Pro Val Leu Pro Gly Gly Leu  
 1 5 10 15  
 Phe Val Ala Leu Gly Trp Ile Phe Leu Leu Phe His Arg Asp Ala Phe  
 20 25 30  
 Ser Leu His Thr Met Ser Ala Gly Phe Pro  
 35 40

&lt;210&gt; 128

&lt;211&gt; 253

&lt;212&gt; PRT

&lt;213&gt; mouse

&lt;400&gt; 128

Met Met Tyr Trp Ile Val Phe Ala Ile Phe Met Ala Ala Glu Thr Phe  
 1 5 10 15  
 Thr Asp Ile Phe Ile Ser Trp Ser Gly Pro Arg Ile Gly Arg Pro Trp  
 20 25 30  
 Gly Trp Glu Gly Pro His His His His His Leu Ala Ser Gly Ser His  
 35 40 45  
 Lys Pro Leu Pro Leu Leu Thr His Arg Phe Pro Phe Tyr Tyr Glu Phe  
 50 55 60  
 Lys Met Ala Phe Val Leu Trp Leu Leu Ser Pro Tyr Thr Lys Gly Ala

65		70		75		80									
Ser	Leu	Leu	Tyr	Arg	Lys	Phe	Val	His	Pro	Ser	Leu	Ser	Arg	His	Glu
			85						90					95	
Lys	Glu	Ile	Asp	Ala	Cys	Ile	Val	Gln	Ala	Lys	Glu	Arg	Ser	Tyr	Glu
			100					105						110	
Thr	Met	Leu	Ser	Phe	Gly	Lys	Arg	Ser	Leu	Asn	Ile	Ala	Ala	Ser	Ala
			115					120						125	
Ala	Val	Gln	Ala	Ala	Thr	Lys	Ser	Gln	Gly	Ala	Leu	Ala	Gly	Arg	Leu
			130					135						140	
Arg	Ser	Phe	Ser	Met	Gln	Asp	Leu	Arg	Ser	Ile	Pro	Asp	Thr	Pro	Val
			145				150				155				160
Pro	Thr	Tyr	Gln	Asp	Pro	Leu	Tyr	Leu	Glu	Asp	Gln	Val	Pro	Arg	Arg
			165						170					175	
Arg	Pro	Pro	Ile	Gly	Tyr	Arg	Pro	Gly	Gly	Leu	Gln	Gly	Ser	Asp	Thr
			180					185						190	
Glu	Asp	Glu	Cys	Trp	Ser	Asp	Asn	Glu	Ile	Val	Pro	Gln	Pro	Pro	Val
			195					200					205		
Arg	Pro	Arg	Glu	Lys	Pro	Leu	Gly	Arg	Ser	Gln	Ser	Leu	Arg	Val	Val
			210				215						220		
Lys	Arg	Lys	Pro	Leu	Thr	Arg	Glu	Gly	Thr	Ser	Arg	Ser	Leu	Lys	Val
			225				230				235				240
Arg	Thr	Arg	Lys	Lys	Ala	Met	Pro	Ser	Asp	Met	Asp	Ser			
			245						250						

<210> 129  
 <211> 40  
 <212> PRT  
 <213> mouse

<400> 129															
Met	Lys	Ala	Met	Ala	Leu	Ser	Leu	Gly	Ala	Ser	Pro	Val	Leu	Ala	Phe
1			5					10					15		
Leu	Leu	Ser	Gly	Tyr	Ser	Asp	Gly	Tyr	Gln	Val	Cys	Ser	Arg	Phe	Gly
			20					25					30		
Ser	Lys	Val	Pro	Gln	Phe	Leu	Asn								
			35				40								

<210> 130  
 <211> 87  
 <212> PRT  
 <213> mouse

<400> 130															
Met	Ile	Ala	Val	Thr	Phe	Ala	Ile	Val	Leu	Gly	Val	Ile	Ile	Tyr	Arg
1			5					10						15	
Ile	Ser	Thr	Ala	Ala	Ala	Leu	Ala	Met	Asn	Ser	Ser	Pro	Ser	Val	Arg
			20					25					30		
Ser	Asn	Ile	Arg	Val	Thr	Val	Thr	Ala	Thr	Ala	Val	Ile	Ile	Asn	Leu
			35				40					45			
Val	Val	Ile	Ile	Leu	Leu	Asp	Glu	Val	Tyr	Gly	Cys	Ile	Ala	Arg	Trp
			50				55				60				
Leu	Thr	Lys	Ile	Gly	Glu	Cys	His	Val	Gln	Asp	Ser	Ile	Gly	Ser	Met
			65				70			75					80
Gly	Leu	Gly	Gln	Gly	Gln	Pro									
			85												

<210> 131  
 <211> 70  
 <212> PRT  
 <213> mouse

<400> 131  
 Met Phe Gly Leu Val His Val Cys Thr Cys Val Cys Val Cys Val Cys  
 1 5 10 15  
 Val Cys Val Cys Val Cys Ile Cys Ser Cys Gly Tyr Val His Val Pro  
 20 25 30  
 Cys Gly Cys Val Cys Leu Trp Gly Pro Glu Val Arg Tyr Leu Pro Leu  
 35 40 45  
 Ser Leu His Pro Gly Gly Phe Cys Phe Val Leu Phe Cys Phe Gly Pro  
 50 55 60  
 Gly Leu Ser Leu Ile Ser  
 65 70

<210> 132  
 <211> 63  
 <212> PRT  
 <213> mouse

<400> 132  
 Met Trp Leu Leu Val Ala Leu Thr Leu Ser Val Tyr Ser Leu Val Ala  
 1 5 10 15  
 Phe Val Thr Gly Met Leu Cys Asp Thr Val Val Ile Lys Met Leu Met  
 20 25 30  
 Ser Leu His Lys Ser Ser Lys Leu Asn Pro Arg Ala Lys Cys Gly Gly  
 35 40 45  
 Val Pro Leu Ile Pro Ala Leu Trp Gly Gln Val Gln Val Val Leu  
 50 55 60

<210> 133  
 <211> 39  
 <212> PRT  
 <213> mouse

<400> 133  
 Met Asp Asn Thr Leu Ser Ile Ile Ile Tyr Leu Leu Phe Ile Phe Ala  
 1 5 10 15  
 Ile Ser Val Leu Asp Ser Gln Leu Ser Thr Arg Cys Leu Trp Trp Phe  
 20 25 30  
 Ser Lys Asp Leu Glu Val Thr  
 35

<210> 134  
 <211> 90  
 <212> PRT  
 <213> Rat

<400> 134  
 Met Pro Thr Met Trp Pro Leu Leu His Val Leu Trp Leu Ala Leu Val  
 1 5 10 15  
 Cys Gly Ser Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala  
 20 25 30  
 Ala Ser Lys Thr Leu Leu Glu Lys Thr Gln Phe Ser Asp Lys Pro Val  
 35 40 45  
 Gln Asp Arg Gly Leu Val Val Thr Asp Ile Lys Ala Glu Asp Val Val  
 50 55 60  
 Leu Glu His Arg Ser Tyr Cys Ser Ala Arg Ala Arg Glu Arg Asn Phe  
 65 70 75 80  
 Ala Gly Glu Val Leu Gly Ile Cys His Ser  
 85 90

<210> 135  
 <211> 193

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 135

Met Thr Ser Gly Pro Gly Gly Pro Ala Ala Ala Thr Gly Gly Gly Lys  
 1 5 10 15  
 Asp Thr His Gln Trp Tyr Val Cys Asn Arg Glu Lys Leu Cys Glu Ser  
 20 25 30  
 Leu Gln Ser Val Phe Val Gln Ser Tyr Leu Asp Gln Gly Thr Gln Ile  
 35 40 45  
 Phe Leu Asn Asn Ser Ile Glu Lys Ser Gly Trp Leu Phe Ile Gln Leu  
 50 55 60  
 Tyr His Ser Phe Val Ser Ser Val Phe Thr Leu Phe Met Ser Arg Thr  
 65 70 75 80  
 Ser Ile Asn Gly Leu Leu Gly Arg Gly Ser Met Phe Val Phe Ser Pro  
 85 90 95  
 Asp Gln Phe Gln Arg Leu Leu Lys Ile Asn Pro Asp Trp Lys Thr His  
 100 105 110  
 Arg Leu Leu Asp Leu Gly Ala Gly Asp Gly Glu Val Thr Lys Ile Met  
 115 120 125  
 Ser Pro His Phe Glu Glu Ile Tyr Ala Thr Glu Leu Ser Glu Thr Met  
 130 135 140  
 Ile Trp Gln Leu Gln Lys Lys Lys Tyr Arg Val Leu Gly Ile Asn Glu  
 145 150 155 160  
 Trp Gln Asn Thr Gly Phe Gln Tyr Asp Val Ile Ser Cys Leu Asn Leu  
 165 170 175  
 Leu Asp Arg Cys Asp Gln Pro Leu Thr Leu Leu Lys Asp Ile Arg Met  
 180 185 190  
 Ser

&lt;210&gt; 136

&lt;211&gt; 106

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 136

Met Ala Ala Pro Met Asp Arg Thr His Gly Gly Arg Ala Ala Arg Ala  
 1 5 10 15  
 Leu Arg Arg Ala Leu Ala Leu Ala Ser Leu Ala Gly Leu Leu Leu Ser  
 20 25 30  
 Gly Leu Ala Gly Ala Leu Pro Thr Leu Gly Pro Gly Trp Arg Arg Gln  
 35 40 45  
 Asn Pro Glu Pro Pro Ala Ser Arg Thr Arg Ser Leu Leu Leu Asp Ala  
 50 55 60  
 Ala Ser Gly Gln Leu Arg Leu Glu Tyr Gly Phe His Pro Asp Ala Val  
 65 70 75 80  
 Ala Trp Ala Asn Leu Thr Asn Ala Ile Arg Glu Thr Gly Trp Ala Tyr  
 85 90 95  
 Leu Asp Leu Gly Thr Asn Gly Ser Tyr Lys  
 100 105

&lt;210&gt; 137

&lt;211&gt; 286

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 137

Met Ala Ala Ala Met Pro Leu Gly Leu Ser Leu Leu Leu Leu Val Leu  
 1 5 10 15  
 Val Gly Gln Gly Cys Cys Gly Arg Val Glu Gly Pro Arg Asp Ser Leu

20 25 30  
 Arg Glu Glu Leu Val Ile Thr Pro Leu Pro Ser Gly Asp Val Ala Ala  
 35 40 45  
 Thr Phe Gln Phe Arg Thr Arg Trp Asp Ser Asp Leu Gln Arg Glu Gly  
 50 55 60  
 Val Ser His Tyr Arg Leu Phe Pro Lys Ala Leu Gly Gln Leu Ile Ser  
 65 70 75 80  
 Lys Tyr Ser Leu Arg Glu Leu His Leu Ser Phe Thr Gln Gly Phe Trp  
 85 90 95  
 Arg Thr Arg Tyr Trp Gly Pro Pro Phe Leu Gln Ala Pro Ser Gly Ala  
 100 105 110  
 Glu Leu Trp Val Trp Phe Gln Asp Thr Val Thr Asp Val Asp Lys Ser  
 115 120 125  
 Trp Lys Glu Leu Ser Asn Val Leu Ser Gly Ile Phe Cys Ala Ser Leu  
 130 135 140  
 Asn Phe Ile Asp Ser Thr Asn Thr Val Thr Pro Thr Ala Ser Phe Lys  
 145 150 155 160  
 Pro Leu Gly Leu Ala Asn Asp Thr Asp His Tyr Phe Leu Arg Tyr Ala  
 165 170 175  
 Val Leu Pro Arg Glu Val Val Cys Thr Glu Asn Leu Thr Pro Trp Lys  
 180 185 190  
 Lys Leu Leu Pro Cys Ser Ser Lys Ala Gly Leu Ser Val Leu Leu Lys  
 195 200 205  
 Ala Asp Arg Leu Phe His Thr Ser Tyr His Ser Gln Ala Val His Ile  
 210 215 220  
 Arg Pro Ile Cys Arg Asn Ala His Cys Thr Ser Ile Ser Trp Glu Leu  
 225 230 235 240  
 Arg Gln Thr Leu Ser Val Val Phe Asp Ala Phe Ile Thr Gly Gln Gly  
 245 250 255  
 Lys Lys Glu Ala Cys Pro Leu Ala Ser Gln Ser Leu Val Tyr Val Asp  
 260 265 270  
 Ile Thr Gly Tyr Ser Gln Asp Asn Glu Thr Leu Glu Val Ser  
 275 280 285

&lt;210&gt; 138

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 138

Met Thr Val Phe Arg Lys Val Thr Thr Met Ile Ser Trp Met Leu Leu  
 1 5 10 15  
 Ala Cys Ala Leu Pro Cys Ala Ala Asp Pro Met Leu Gly Ala Phe Ala  
 20 25 30  
 Arg Arg Asp Phe Gln Lys Gly Gly Pro Gln Leu Val Cys Ser Leu Pro  
 35 40 45  
 Gly Pro Gln Gly Pro Pro Gly Pro Pro Gly Ala Pro Gly Ser Ser Gly  
 50 55 60  
 Met Val Gly Arg Met Gly Phe Pro Gly Lys Asp Gly Gln Asp Gly Gln  
 65 70 75 80  
 Asp Gly Asp Arg Gly Asp Ser Gly Glu Glu Gly Pro Pro Gly Arg Thr  
 85 90 95  
 Gly Asn Arg Gly Lys Gln Gly Pro Lys Gly Lys Ala Gly Ala Ile Gly  
 100 105 110  
 Arg Ala Gly Pro Arg Gly Pro Lys Gly Val Ser Gly Thr Pro Gly Lys  
 115 120 125  
 His Gly Ile Pro Gly Lys Lys Gly Pro Lys Gly Lys Lys Gly Glu Pro  
 130 135 140  
 Gly Leu Pro Gly Pro Cys Ser Cys Gly Ser Ser Arg Ala Lys Ser Ala  
 145 150 155 160  
 Phe Ser Val Ala Val Thr Lys Ser Tyr Pro Arg Glu Arg Leu Pro Ile

```
<210> 139
<211> 233
<212> PRT
<213> Rat
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<210>	140
<211>	38
<212>	PRT
<213>	Human

```
<210> 141
<211> 322
<212> PRT
<213> mouse
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&lt;400&gt; 141

```

Met Asp Ala Arg Trp Trp Ala Val Val Val Leu Ala Thr Leu Pro Ser
 1           5           10           15
Leu Gly Ala Gly Gly Glu Ser Pro Glu Ala Pro Pro Gln Ser Trp Thr
           20           25           30
Gln Leu Trp Leu Phe Arg Phe Leu Leu Asn Val Ala Gly Tyr Ala Ser
           35           40           45
Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Leu Arg Arg Lys Asn
           50           55           60
Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys
65           70           75           80
Val Phe Gly Asn Glu Pro Lys Ala Pro Asp Glu Val Leu Leu Ala Pro
           85           90           95
Arg Thr Glu Thr Ala Glu Ser Thr Pro Ser Trp Gln Val Leu Lys Leu
           100          105          110
Val Phe Cys Ala Ser Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Ile
           115          120          125
Leu Gln Glu Arg Val Met Thr Gly Ser Tyr Gly Ala Thr Ala Thr Ser
           130          135          140
Pro Gly Glu His Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg
145          150          155          160
Val Leu Ala Leu Val Val Ala Gly Leu Tyr Cys Val Leu Arg Lys Gln
           165          170          175
Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser
           180          185          190
Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser
           195          200          205
Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met
210          215          220
Met Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr
225          230          235          240
Leu Thr Ala Gly Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser
           245          250          255
Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu
           260          265          270
Val Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp
           275          280          285
Gln Asp Ala Leu Phe Ala Tyr Lys Met Ser Ser Val Gln Met Met Phe
290          295          300
Gly Val Asn Leu Phe Ser Cys Leu Phe Thr Val Gly Ser Leu Leu Glu
305          310          315          320
Gln Gly

```

&lt;210&gt; 142

&lt;211&gt; 312

&lt;212&gt; PRT

&lt;213&gt; mouse

&lt;400&gt; 142

```

Met Leu Cys Leu Cys Leu Tyr Val Pro Ile Ala Gly Ala Ala Gln Thr
 1           5           10           15
Glu Phe Gln Tyr Phe Glu Ser Lys Gly Leu Pro Ala Glu Leu Lys Ser
           20           25           30
Ile Phe Lys Leu Ser Val Phe Ile Pro Ser Gln Glu Phe Ser Thr Tyr
           35           40           45
Arg Gln Trp Lys Gln Lys Ile Val Gln Ala Gly Asp Lys Asp Leu Asp
50           55           60
Gly Gln Leu Asp Phe Glu Glu Phe Val His Tyr Leu Gln Asp His Glu
65           70           75           80
Lys Lys Leu Arg Leu Val Phe Lys Ser Leu Asp Lys Lys Asn Asp Gly

```

```
<210> 143
<211> 163
<212> PRT
<213> Rat
```

<210> 144  
<211> 330

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 144

Met Ala Gly Trp Ala Gly Ala Glu Leu Ser Val Leu Asn Pro Leu Arg  
 1 5 10 15  
 Ala Leu Trp Leu Leu Leu Ala Ala Ala Phe Leu Leu Ala Leu Leu  
 20 25 30  
 Gln Leu Ala Pro Ala Arg Leu Leu Pro Ser Cys Ala Leu Phe Gln Asp  
 35 40 45  
 Leu Ile Arg Tyr Gly Lys Thr Lys Gln Ser Gly Ser Arg Arg Pro Ala  
 50 55 60  
 Val Cys Arg Ala Phe Asp Val Pro Lys Arg Tyr Phe Ser His Phe Tyr  
 65 70 75 80  
 Val Val Ser Val Leu Trp Asn Gly Ser Leu Leu Trp Phe Leu Ser Gln  
 85 90 95  
 Ser Leu Phe Leu Gly Ala Pro Phe Pro Ser Trp Leu Trp Ala Leu Leu  
 100 105 110  
 Arg Thr Leu Gly Val Thr Gln Phe Gln Ala Leu Gly Met Glu Ser Lys  
 115 120 125  
 Ala Ser Arg Ile Gln Ala Gly Glu Leu Ala Leu Ser Thr Phe Leu Val  
 130 135 140  
 Leu Val Phe Leu Trp Val His Ser Leu Arg Arg Leu Phe Glu Cys Phe  
 145 150 155 160  
 Tyr Val Ser Val Phe Ser Asn Thr Ala Ile His Val Val Gln Tyr Cys  
 165 170 175  
 Phe Gly Leu Val Tyr Tyr Val Leu Val Gly Leu Thr Val Leu Ser Gln  
 180 185 190  
 Val Pro Met Asn Asp Lys Asn Val Tyr Ala Leu Gly Lys Asn Leu Leu  
 195 200 205  
 Leu Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Met Phe Phe Trp  
 210 215 220  
 Ser Ser Ala His Gln Tyr Lys Cys His Val Ile Leu Ser Asn Leu Arg  
 225 230 235 240  
 Arg Asn Lys Lys Gly Val Val Ile His Cys Gln His Arg Ile Pro Phe  
 245 250 255  
 Gly Asp Trp Phe Glu Tyr Val Ser Ser Ala Asn Tyr Leu Ala Glu Leu  
 260 265 270  
 Met Ile Tyr Ile Ser Met Ala Val Thr Phe Gly Leu His Asn Val Thr  
 275 280 285  
 Trp Trp Leu Val Val Thr Tyr Val Phe Phe Ser Gln Ala Leu Ser Ala  
 290 295 300  
 Phe Phe Asn His Arg Phe Tyr Lys Ser Thr Phe Val Ser Tyr Pro Lys  
 305 310 315 320  
 His Arg Lys Ala Phe Leu Pro Phe Leu Phe  
 325 330

&lt;210&gt; 145

&lt;211&gt; 301

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 145

Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly  
 1 5 10 15  
 Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser  
 20 25 30  
 Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu  
 35 40 45  
 Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr  
 50 55 60

Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val  
 65 70 75 80  
 Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile  
 85 90 95  
 Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr  
 100 105 110  
 Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn  
 115 120 125  
 Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg  
 130 135 140  
 Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu  
 145 150 155 160  
 Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser  
 165 170 175  
 Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe  
 180 185 190  
 Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp  
 195 200 205  
 Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser  
 210 215 220  
 Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys  
 225 230 235 240  
 Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu  
 245 250 255  
 Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu  
 260 265 270  
 Gln Arg Cys Leu Leu Gly Leu Pro Val Trp Glu Gly Ser Pro His Leu  
 275 280 285  
 Pro Thr Gly His Trp Leu Arg Glu Leu Trp Ser Leu Leu  
 290 295 300

&lt;210&gt; 146

&lt;211&gt; 61

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 146

Met Glu Asn Ile Tyr Tyr Thr Asn Leu Ile Thr Ile Leu Gly Asn Lys  
 1 5 10 15  
 His Ala Asn Gln Met Glu Leu Asn Leu Gln Ala Leu Ile Leu Ser Pro  
 20 25 30  
 Trp Phe Ala Val Cys Ala Pro Pro Gly Phe Ala Arg Asp Gln Ala Val  
 35 40 45  
 Arg Gly Leu Ala Leu Ala Gly Arg Arg Ile Thr Val Val  
 50 55 60

&lt;210&gt; 147

&lt;211&gt; 105

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 147

Met Leu Arg Arg Gln Leu Val Trp Trp His Leu Leu Ala Leu Leu Phe  
 1 5 10 15  
 Leu Pro Phe Cys Leu Cys Gln Asp Glu Tyr Met Glu Ser Pro Gln Ala  
 20 25 30  
 Gly Gly Leu Pro Pro Asp Cys Ser Lys Cys Cys His Gly Asp Tyr Gly  
 35 40 45  
 Phe Arg Gly Tyr Gln Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Ile  
 50 55 60  
 Pro Gly Asn His Gly Asn Asn Gly Asn Asn Gly Ala Thr Gly His Glu

65 70 75 80  
 Gly Ala Lys Gly Glu Lys Gly Asp Lys Gly Asp Leu Gly Pro Arg Gly  
 85 90 95  
 Glu Arg Gly Gln His Gly Pro Lys Gly  
 100 105

<210> 148  
 <211> 210  
 <212> PRT  
 <213> Rat

<400> 148  
 Met Leu Gly Ala Thr Ser Leu Ser Trp Pro Trp Val Leu Trp Ala Val  
 1 5 10 15  
 Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu Gly Gly Leu  
 20 25 30  
 Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile Phe Tyr Ser  
 35 40 45  
 Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly Met Ala Ile  
 50 55 60  
 Phe Ser Leu Leu Leu Gln Ala Leu Leu Leu Leu Pro Arg Leu Pro His  
 65 70 75 80  
 Ala Pro Gly Ser Glu Gly Val Ser Ser Arg Ser Ala Arg Ile Ser Ser  
 85 90 95  
 Asp Leu Leu Arg Asn Ile Val Pro Thr Arg Gln Leu Thr Arg Gln Thr  
 100 105 110  
 His Leu Gln Thr Pro Leu Gln Ala Trp Arg Thr Arg Ala Lys Leu Pro  
 115 120 125  
 Pro Gly Gly Thr Glu Ala Val Pro Gly Arg Pro Gly Ala Gln Gln Asp  
 130 135 140  
 Ala Cys His Leu Leu Tyr Trp Thr Tyr Asn Gly Val Ser Ser Ile Pro  
 145 150 155 160  
 Cys His Arg Gly Gly Leu Ser His Val Pro Ser Glu Val Pro Ala Glu  
 165 170 175  
 Lys Ser Pro Val Leu Ile Leu His Ala Ala Pro Pro Phe Lys Thr Pro  
 180 185 190  
 Val Asn Pro Trp Ala Arg Thr Val Val Gly Phe Phe Pro Ser Ser Pro  
 195 200 205  
 Ser Leu  
 210

<210> 149  
 <211> 301  
 <212> PRT  
 <213> Rat

<400> 149  
 Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly  
 1 5 10 15  
 Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser  
 20 25 30  
 Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu  
 35 40 45  
 Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr  
 50 55 60  
 Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val  
 65 70 75 80  
 Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile  
 85 90 95  
 Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr  
 100 105 110

Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn  
 115 120 125  
 Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg  
 130 135 140  
 Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu  
 145 150 155 160  
 Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser  
 165 170 175  
 Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe  
 180 185 190  
 Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp  
 195 200 205  
 Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser  
 210 215 220  
 Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys  
 225 230 235 240  
 Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu  
 245 250 255  
 Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu  
 260 265 270  
 Gln Arg Cys Leu Leu Gly Leu Pro Val Trp Glu Gly Ser Pro His Leu  
 275 280 285  
 Pro Thr Gly His Trp Leu Arg Glu Leu Trp Ser Leu Leu  
 290 295 300

<210> 150  
 <211> 80  
 <212> PRT  
 <213> Human

<400> 150  
 Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys  
 1 5 10 15  
 Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu  
 20 25 30  
 Phe Gln Asp Thr Lys Val Tyr Cys Thr Arg Glu Ser Asn Pro His Cys  
 35 40 45  
 Gly Ser Asp Gly Gln Thr Tyr Gly Asn Lys Cys Ala Phe Cys Lys Ala  
 50 55 60  
 Ile Val Lys Ser Gly Gly Lys Ile Ser Leu Lys His Pro Gly Lys Cys  
 65 70 75 80

<210> 151  
 <211> 27  
 <212> PRT  
 <213> mouse

<400> 151  
 Met Leu Lys Ala Ser Leu His Ile Leu Phe Leu Gly Ile Leu Asn Val  
 1 5 10 15  
 Pro Ile Val Asp Thr Ser Thr Lys Thr Gly Val  
 20 25

<210> 152  
 <211> 86  
 <212> PRT  
 <213> mouse

<400> 152  
 Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile  
 1 5 10 15

Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser  
                   20                                  25                                  30  
 Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala  
                   35                                  40                                  45  
 Gly Ala Gln Gly Met Trp Gly Ile Trp Gly His Thr Ile Thr Cys Gly  
                   50                                  55                                  60  
 Leu Ala Pro Gly Ala Lys Pro Cys Ser Leu Lys Arg Glu Gly Pro Asp  
                   65                                  70                                  75                                  80  
 Leu Leu Ser Phe Pro Pro  
   85

<210> 153  
 <211> 72  
 <212> PRT  
 <213> mouse

<400> 153  
 Met Ser Ala Ile Phe Asn Phe Gln Ser Leu Leu Thr Val Ile Leu Leu  
   1                                  5                                  10                                  15  
 Leu Ile Cys Thr Cys Ala Tyr Ile Arg Ser Leu Ala Pro Ser Ile Leu  
                   20                                  25                                  30  
 Asp Arg Asn Lys Thr Gly Leu Leu Gly Ile Phe Trp Lys Cys Ala Arg  
                   35                                  40                                  45  
 Ile Gly Glu Arg Lys Ser Pro Tyr Val Ala Ile Cys Cys Ile Val Met  
                   50                                  55                                  60  
 Ala Phe Ser Ile Leu Phe Ile Gln  
   65                                  70

<210> 154  
 <211> 169  
 <212> PRT  
 <213> mouse

<400> 154  
 Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly  
   1                                  5                                  10                                  15  
 Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg  
                   20                                  25                                  30  
 Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly  
                   35                                  40                                  45  
 Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln  
                   50                                  55                                  60  
 Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu  
   65                                  70                                  75                                  80  
 Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr  
                                   85                                  90                                  95  
 Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly  
                   100                                  105                                  110  
 Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe  
                   115                                  120                                  125  
 Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu  
                   130                                  135                                  140  
 Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu  
   145                                  150                                  155                                  160  
 Gly Glu Met Pro Pro Glu Asp Gly Met  
   165

<210> 155  
 <211> 61  
 <212> PRT  
 <213> mouse

<400> 155  
 Met Glu Lys Gln Met Asp Ala Ser Val Ser Val Ile Phe Gly Ser Ile  
 1 5 10 15  
 Val Ile Ser Ala Phe Leu Tyr Leu Ser Leu Ala Gly Pro Trp Ala Val  
 20 25 30  
 Thr Val Thr Gln Met Arg Thr Ile Ile Ile Thr Met Asp Gln Leu Arg  
 35 40 45  
 Asp Ala Leu Ile Leu Asp Gln Leu Lys Val Ala Val Ser  
 50 55 60

<210> 156  
 <211> 131  
 <212> PRT  
 <213> mouse

<400> 156  
 Met Ala Pro Ser Leu Trp Lys Gly Leu Val Gly Val Gly Leu Phe Ala  
 1 5 10 15  
 Leu Ala His Ala Ala Phe Ser Ala Ala Gln His Arg Ser Tyr Met Arg  
 20 25 30  
 Leu Thr Glu Lys Glu Asp Glu Ser Leu Pro Ile Asp Ile Val Leu Gln  
 35 40 45  
 Thr Leu Leu Ala Phe Ala Val Thr Cys Tyr Gly Ile Val His Ile Ala  
 50 55 60  
 Gly Glu Phe Lys Asp Met Asp Ala Thr Ser Glu Leu Lys Asn Lys Thr  
 65 70 75 80  
 Phe Asp Thr Leu Arg Asn His Pro Ser Phe Tyr Val Phe Asn His Arg  
 85 90 95  
 Gly Arg Val Leu Phe Arg Pro Ser Asp Ala Thr Asn Ser Ser Asn Leu  
 100 105 110  
 Asp Ala Leu Ser Ser Asn Thr Ser Leu Lys Leu Arg Lys Phe Asp Ser  
 115 120 125  
 Leu Arg Arg  
 130

<210> 157  
 <211> 133  
 <212> PRT  
 <213> mouse

<400> 157  
 Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Ala Leu Cys  
 1 5 10 15  
 Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro  
 20 25 30  
 Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr  
 35 40 45  
 Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Glu His Val  
 50 55 60  
 Gln Gly Thr Gly Ala Arg Ser Thr Ala Cys Thr Leu Ser Cys Arg Ala  
 65 70 75 80  
 Pro Asn Ala Ser Ser Ser Gly Thr Met Pro Gly Thr Arg Ser Ala Gly  
 85 90 95  
 Ser Thr Lys Asn Arg Val Asp Asp His Gly Lys Lys Asn Ser Arg Pro  
 100 105 110  
 Val Glu Arg Leu Gln Gln Arg Thr Leu Gln Ile Lys Ile Lys Ala Leu  
 115 120 125  
 Ser Phe Ser Gln Ala  
 130



<210> 158  
 <211> 78  
 <212> PRT  
 <213> mouse

<400> 158  
 Gly Thr Arg Lys Pro Leu Pro Met Glu Ala His Ser Arg Arg Glu Lys  
 1 5 10 15  
 Ala Ser Gly Leu Arg Leu Ala Trp His Tyr Glu Cys Ser Gly Val Ser  
 20 25 30  
 Val Trp Trp Met Cys Val Leu Gly Trp Leu Ser Phe Leu Val Phe Leu  
 35 40 45  
 Leu Phe Ser Leu Val Cys Ser Phe Pro Ser Pro Ile Asn His Ser His  
 50 55 60  
 Met Leu Pro Cys Leu Phe Leu Arg Gly Gly Gly Ser Asn Val  
 65 70 75

<210> 159  
 <211> 206  
 <212> PRT  
 <213> mouse

<400> 159  
 Met Leu Pro Pro Ala Ile His Leu Ser Leu Ile Pro Leu Leu Cys Ile  
 1 5 10 15  
 Leu Met Arg Asn Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu  
 20 25 30  
 Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser  
 35 40 45  
 Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Ser Thr Gly  
 50 55 60  
 Leu Asp Arg Asn Ser Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser  
 65 70 75 80  
 Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys  
 85 90 95  
 Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn  
 100 105 110  
 Trp Ile Gly Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser  
 115 120 125  
 Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln  
 130 135 140  
 Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val  
 145 150 155 160  
 Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Ser  
 165 170 175  
 His Asn Phe Glu Ser Val Ser Pro Ala Lys Pro Ala Gln His His Arg  
 180 185 190  
 Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Leu Ser  
 195 200 205

<210> 160  
 <211> 169  
 <212> PRT  
 <213> mouse

<400> 160  
 Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly  
 1 5 10 15  
 Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg  
 20 25 30  
 Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly

35 40 45  
 Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln  
 50 55 60  
 Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu  
 65 70 75 80  
 Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr  
 85 90 95  
 Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly  
 100 105 110  
 Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe  
 115 120 125  
 Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu  
 130 135 140  
 Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu  
 145 150 155 160  
 Gly Glu Met Pro Pro Glu Asp Gly Met  
 165

<210> 161  
 <211> 114  
 <212> PRT  
 <213> mouse

<400> 161  
 Met Ser Val Thr Ile Gly Arg Leu Ala Leu Phe Leu Ile Gly Ile Leu  
 1 5 10 15  
 Leu Cys Pro Val Ala Pro Ser Leu Thr Arg Ser Trp Pro Gly Pro Asp  
 20 25 30  
 Thr Cys Ser Leu Phe Leu Gln His Ser Leu Ser Leu Ser Leu Arg Leu  
 35 40 45  
 Gly Gln Ser Leu Glu Gly Gly Leu Ser Val Cys Phe His Val Cys Ile  
 50 55 60  
 His Ala Cys Glu Cys Val Ala Cys Cys Arg Val Leu Trp Asp Pro Lys  
 65 70 75 80  
 Pro Arg Gly Ser Ser Leu Cys Arg Trp Val Leu Gly Ser Ile Thr Cys  
 85 90 95  
 Leu Phe Met Tyr Glu Val Gly Gly Trp Thr Gln Gly Gly Leu Ile Val  
 100 105 110  
 Ser Leu

<210> 162  
 <211> 46  
 <212> PRT  
 <213> mouse

<400> 162  
 Met His Tyr Pro Cys Leu Ala Cys Leu Phe Val Asn Val His Trp Cys  
 1 5 10 15  
 Phe Ala Trp Met Cys Ile Leu Val Lys Met Ser Glu Leu Leu Glu Leu  
 20 25 30  
 Glu Leu Glu Thr Met Val Ser Cys Leu Val Asp Val Gly Asn  
 35 40 45

<210> 163  
 <211> 122  
 <212> PRT  
 <213> mouse

<400> 163  
 Met Phe Thr Phe Val Val Leu Val Ile Thr Ile Val Ile Cys Leu Cys

1                      5                      10                      15  
 His Val Cys Phe Gly His Phe Lys Tyr Leu Ser Ala His Asn Tyr Lys  
                     20                      25                      30  
 Ile Glu His Thr Glu Thr Asp Ala Val Ser Ser Arg Ser Asn Gly Arg  
                     35                      40                      45  
 Pro Pro Thr Ala Gly Ala Val Pro Lys Ser Ala Lys Tyr Ile Ala Gln  
                     50                      55                      60  
 Val Leu Gln Asp Ser Glu Gly Asp Gly Asp Gly Ala Pro Gly  
 65                      70                      75                      80  
 Ser Ser Gly Asp Glu Pro Pro Ser Ser Ser Ser Gln Asp Glu Glu Leu  
                     85                      90                      95  
 Leu Met Pro Pro Asp Gly Leu Thr Asp Thr Asp Phe Gln Ser Cys Glu  
                     100                      105                      110  
 Asp Ser Leu Ile Glu Asn Glu Ile His Gln  
                     115                      120

&lt;210&gt; 164

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 164

Met Ser Phe Val Lys Ile Glu Ala Thr Pro Thr Gln Thr Lys Trp Pro  
 1                      5                      10                      15  
 Phe Ser Val Val Pro Gln Ser Leu Leu Val Thr Val Tyr Ile Cys Tyr  
                     20                      25                      30  
 Ile Phe Leu Val Ile Phe Phe Phe Phe Glu Ala Cys Gln Glu Val  
                     35                      40                      45  
 Leu Cys Ser Phe Phe Asp Phe Ser Arg Arg Arg Gly  
                     50                      55                      60

&lt;210&gt; 165

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; mouse

&lt;400&gt; 165

Met Gly Ser Pro Ile Ser Gly Val Cys Pro Val Leu Pro Gly Gly Leu  
 1                      5                      10                      15  
 Phe Val Ala Leu Gly Trp Ile Phe Leu Leu Phe His Arg Asp Ala Phe  
                     20                      25                      30  
 Ser Leu His Thr Met Ser Ala Gly Phe Pro Lys Ser Pro Ala Asn Pro  
                     35                      40                      45  
 His His Pro Pro Leu Arg Leu Ser Pro  
                     50                      55

&lt;210&gt; 166

&lt;211&gt; 75

&lt;212&gt; PRT

&lt;213&gt; mouse

&lt;400&gt; 166

Lys Thr Arg Arg Thr Leu Thr Gly Gln Leu Gly Leu Phe Ser Val Asp  
 1                      5                      10                      15  
 Phe Met Val Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro  
                     20                      25                      30  
 Phe Pro Leu Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys  
                     35                      40                      45  
 Gln Trp Glu Gly Ser Thr Met Thr His Thr His Thr His Thr His Ile  
                     50                      55                      60  
 His Ile His Thr Pro Pro Arg Gln Cys Gln Ser

65

70

75

<210> 167  
 <211> 52  
 <212> PRT  
 <213> mouse

<400> 167  
 Val Arg Ser Leu Glu Gln Leu Gly Leu Phe Ser Val Asp Phe Met Val  
 1 5 10 15  
 Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro Phe Pro Leu  
 20 25 30  
 Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys Gln Trp Glu  
 35 40 45  
 Gly Ser Thr Met  
 50

<210> 168  
 <211> 119  
 <212> PRT  
 <213> Rat

<400> 168  
 Met Leu Gly Ala Thr Ser Leu Ser Trp Pro Trp Val Leu Trp Ala Val  
 1 5 10 15  
 Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu Gly Gly Leu  
 20 25 30  
 Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile Phe Tyr Ser  
 35 40 45  
 Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly Met Ala Ile  
 50 55 60  
 Phe Ser Leu Leu Leu Gln Ala Leu Leu Leu Leu Pro Arg Leu Pro His  
 65 70 75 80  
 Ala Pro Gly Ser Glu Gly Val Ser Ser Arg Ser Ala Arg Ile Ser Ser  
 85 90 95  
 Asp Leu Leu Arg Asn Ile Val Pro Thr Arg Gln Leu Thr Arg Gln Thr  
 100 105 110  
 His Leu Gln Thr Pro Leu Gln  
 115

<210> 169  
 <211> 104  
 <212> PRT  
 <213> Rat

<220>

<400> 169  
 Leu Val Pro Lys Ser Ala Arg Ala Ser Leu Leu Cys Cys Gly Pro Lys  
 1 5 10 15  
 Leu Ala Ala Cys Gly Ile Val Leu Ser Ala Trp Gly Val Ile Met Leu  
 20 25 30  
 Ile Met Leu Gly Ile Phe Phe Asn Val His Ser Ala Val Xaa Ile Xaa  
 35 40 45  
 Asp Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile  
 50 55 60  
 Tyr Asn Leu Tyr Glu Gln Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly  
 65 70 75 80  
 Leu Tyr Leu Leu Xaa Gly Gly Phe Ser Phe Cys Gln Val Arg Leu Asn  
 85 90 95

Lys Arg Lys Glu Tyr Met Val Arg  
100

<210> 170  
<211> 123  
<212> PRT  
<213> Rat

<220>  
<221> UNSURE  
<222> (27)...(27)

<221> UNSURE  
<222> (104)...(104)

<221> UNSURE  
<222> (118)...(118)

<400> 170  
Met Arg Pro Gly Ala Asp Trp Ala Ala Val Cys Ala Leu Trp Pro Ser  
1 5 10 15  
Trp Arg Pro Ser Cys Ser Leu Pro Ser Ser Xaa Arg Ile Gln Pro Asp  
20 25 30  
Gln Leu Trp Leu Tyr Arg Asn Pro Tyr Val Lys Ala Glu Tyr Phe Pro  
35 40 45  
Thr Gly Pro Met Phe Val Ile Ala Phe Leu Thr Pro Leu Ser Leu Ile  
50 55 60  
Phe Phe Ala Lys Phe Leu Arg Lys Ala Asp Ala Arg Gln Arg Ala  
65 70 75 80  
Ser Leu Pro Arg Cys Gln Pro Cys Pro Ser Ala Lys Trp Cys Leu Tyr  
85 90 95  
Gln His His Lys Thr Asp Ser Xaa Gln Gly His Ala Gln Ile Ala Ser  
100 105 110  
Thr Glu Cys Ser Pro Xaa Gly Ile Ala His Ser  
115 120

<210> 171  
<211> 75  
<212> PRT  
<213> Rat

<400> 171  
Ser Ala Gly Val Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile  
1 5 10 15  
Ala Phe Gly Pro Ala Leu Ser Leu Tyr Val Phe Thr Ile Ala Thr Asp  
20 25 30  
Pro Leu Arg Val Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val  
35 40 45  
Ser Leu Leu Leu Ser Ser Val Phe Trp Phe Leu Val Arg Val Ile Thr  
50 55 60  
Asp Asn Arg Asp Gly Pro Val Gln Asn Tyr Leu  
65 70 75

<210> 172  
<211> 79  
<212> PRT  
<213> Human

<400> 172  
Lys Thr Ser Tyr His Tyr His Thr Asn Val Glu Glu Leu Thr Ile Pro  
1 5 10 15

Glu Thr Arg Asn Asn Leu Tyr Ile Ser Ile Ser Trp Leu Trp Cys Leu  
                   20                  25                  30  
 Val Leu Val Leu Leu Ser Thr Met Ile Leu Asn Lys His Gly Trp Met  
                   35                  40                  45  
 Lys Ala Asn Ala Tyr Ser Leu Val Pro Ser Ile Ile Tyr Ser Pro Ser  
                   50                  55                  60  
 Tyr Leu Lys Leu Leu Leu Arg Leu Tyr Lys Leu Gln Ile Cys Cys  
                   65                  70                  75

<210> 173  
 <211> 134  
 <212> PRT  
 <213> Human

<220>

<400> 173

Leu Arg Gly Arg Gly Val Cys Ser Gln Glu Ser Phe Gly Gly  
   1                  5                  10                  15  
 Cys Cys Val Ser Gly Leu Ile Ala Met Gly Thr Lys Ala Gln Val Glu  
                   20                  25                  30  
 Arg Lys Leu Leu Cys Leu Phe Ile Leu Ala Ile Leu Leu Cys Ser Leu  
                   35                  40                  45  
 Ala Leu Gly Ser Val Thr Val His Ser Ser Glu Pro Glu Val Arg Ile  
                   50                  55                  60  
 Pro Glu Asn Asn Pro Val Lys Leu Ser Cys Ala Tyr Ser Gly Phe Ser  
   65                  70                  75                  80  
 Ser Pro Arg Val Glu Trp Lys Phe Asp Gln Gly Asp Thr Thr Arg Leu  
                   85                  90                  95  
 Val Cys Tyr Asn Asn Lys Ile Thr Ala Ser Tyr Glu Asp Arg Val Thr  
                   100                  105                  110  
 Phe Leu Pro Thr Gly Ile Thr Phe Lys Ser Val Thr Arg Glu Asp Thr  
                   115                  120                  125  
 Gly Thr Tyr Thr Cys Met  
                   130

<210> 174  
 <211> 137  
 <212> PRT  
 <213> Human

<400> 174

Ala Trp Ser Arg Pro Arg Tyr Asp Ser Val Leu Ala Leu Ser Ala Ala  
   1                  5                  10                  15  
 Leu Gln Ala Thr Arg Ala Leu Met Val Val Ser Leu Val Leu Gly Phe  
                   20                  25                  30  
 Leu Ala Met Phe Val Ala Thr Met Gly Met Lys Cys Thr Arg Cys Gly  
                   35                  40                  45  
 Gly Asp Asp Lys Val Lys Lys Ala Arg Ile Ala Met Gly Gly Gly Ile  
                   50                  55                  60  
 Ile Phe Ile Val Ala Gly Leu Ala Ala Leu Val Ala Cys Ser Trp Tyr  
   65                  70                  75                  80  
 Gly His Gln Ile Val Thr Asp Phe Tyr Asn Pro Leu Ile Pro Thr Asn  
                   85                  90                  95  
 Ile Lys Tyr Glu Phe Gly Pro Ala Ile Phe Ile Gly Trp Ala Gly Ser  
                   100                  105                  110  
 Ala Leu Val Ile Leu Gly Gly Ala Leu Ser Pro Val Pro Val Leu Gly  
                   115                  120                  125  
 Ile Arg Ala Gly Leu Gly Thr Cys Pro  
                   130                  135

<210> 175

<211> 43  
 <212> PRT  
 <213> Human

<400> 175  
 Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys  
 1 5 10 15  
 Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu  
 20 25 30  
 Ser Arg Thr Pro Arg Pro Thr Ala Leu Gly Asn  
 35 40

<210> 176  
 <211> 63  
 <212> PRT  
 <213> Rat

<400> 176  
 Pro Asn Thr Arg Pro Arg Arg His Thr Ala Cys Arg Val Ser Ile Ser  
 1 5 10 15  
 Val Phe Tyr Met Leu His Thr Glu Leu Lys Lys Cys Trp Phe Phe Leu  
 20 25 30  
 Phe Cys Phe Ser Leu Phe Leu Trp Phe Cys Phe Trp Phe Cys Phe Leu  
 35 40 45  
 Leu Pro Arg Phe Asp Tyr Leu Pro Met Pro Ser Thr Arg Pro Arg  
 50 55 60

<210> 177  
 <211> 52  
 <212> PRT  
 <213> mouse

<400> 177  
 Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile  
 1 5 10 15  
 Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser  
 20 25 30  
 Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala  
 35 40 45  
 Gly Ala Gln Gly  
 50

<210> 178  
 <211> 62  
 <212> PRT  
 <213> mouse

<400> 178  
 Val Ser Pro Arg Pro Thr Tyr Pro Ser Thr Ala Ser Ser Met Ala Ala  
 1 5 10 15  
 Phe Leu Val Thr Gly Phe Phe Phe Ser Leu Phe Val Val Leu Gly Met  
 20 25 30  
 Glu Pro Arg Ala Leu Phe Arg Pro Asp Lys Ala Leu Pro Leu Ser Cys  
 35 40 45  
 Ala Lys Pro Thr Ser Leu Cys Val Gln Ser Ser Phe Leu Gly  
 50 55 60

<210> 179  
 <211> 123  
 <212> PRT  
 <213> mouse

<400> 179  
 Ala Ser Arg Thr Ala Val Met Ser Leu Cys Arg Cys Gln Gln Gly Ser  
 1 5 10 15  
 Arg Ser Arg Met Asp Leu Asp Val Val Asn Met Phe Val Ile Ala Gly  
 20 25 30  
 Gly Thr Leu Ala Ile Pro Ile Leu Ala Phe Val Ala Ser Phe Leu Leu  
 35 40 45  
 Trp Pro Ser Ala Leu Ile Arg Ile Tyr Tyr Trp Tyr Trp Arg Arg Thr  
 50 55 60  
 Leu Gly Met Gln Val Arg Tyr Ala His His Glu Asp Tyr Gln Phe Cys  
 65 70 75 80  
 Tyr Ser Phe Arg Gly Arg Pro Gly His Lys Pro Ser Ile Leu Met Leu  
 85 90 95  
 His Gly Phe Ser Ala His Lys Gly His Val Ala Gln Arg Gly Gln Val  
 100 105 110  
 Pro Ser Arg Lys Asn Leu His Phe Gly Cys Val  
 115 120

<210> 180  
 <211> 120  
 <212> PRT  
 <213> mouse

<220>  
 <221> UNSURE  
 <222> (5)...(5)

<400> 180  
 Ala Arg Arg Arg Xaa Arg Trp Arg Arg Gly Cys Cys Trp Leu Ile Gly  
 1 5 10 15  
 Thr Gly Leu Arg Ala Ala Thr Trp Thr Val Leu Cys Ser Pro Asn Ser  
 20 25 30  
 Ser Leu Val Val Ala Arg His Thr Lys Ser Phe Pro Pro Lys Lys Pro  
 35 40 45  
 Leu Gln Ala Leu Thr Met Ser Ile Met Asp His Ser Pro Thr Thr Gly  
 50 55 60  
 Val Val Thr Val Ile Val Ile Leu Ile Ala Ile Ala Ala Leu Gly Gly  
 65 70 75 80  
 Leu Ile Leu Gly Cys Trp Cys Tyr Leu Arg Leu Gln Arg Ile Ser Gln  
 85 90 95  
 Ser Glu Asp Glu Glu Ser Ile Val Gly Asp Gly Glu Thr Lys Glu Pro  
 100 105 110  
 Phe Tyr Trp Cys Ser Thr Leu Leu  
 115 120

<210> 181  
 <211> 60  
 <212> PRT  
 <213> mouse

<400> 181  
 Lys Gly Pro Glu Val Ser Cys Cys Ile Lys Tyr Phe Ile Phe Gly Phe  
 1 5 10 15  
 Asn Val Ile Phe Trp Phe Leu Gly Ile Thr Phe Leu Gly Ile Gly Leu  
 20 25 30  
 Trp Ala Trp Asn Glu Lys Gly Val Leu Ser Asn Ile Ser Ser Ile Thr  
 35 40 45  
 Asp Leu Gly Gly Phe Asp Pro Val Trp Leu Phe Leu  
 50 55 60



<210> 182  
 <211> 72  
 <212> PRT  
 <213> mouse

<220>

<400> 182  
 Lys Pro Thr Val Gly Ser Ala Glu Val Ala Ile Ala Val Phe Leu Val  
 1 5 10 15  
 Ile Cys Ile Ile Val Val Leu Thr Ile Leu Gly Tyr Cys Phe Phe Lys  
 20 25 30  
 Asn Gln Arg Lys Glu Phe His Ser Pro Leu His His Pro Pro Pro Thr  
 35 40 45  
 Pro Ala Ser Ser Thr Val Ser Thr Thr Glu Asp Thr Glu His Leu Val  
 50 55 60  
 Tyr Asn His Thr Thr Gln Pro Leu  
 65 70

<210> 183  
 <211> 771  
 <212> PRT  
 <213> Rat

<220>

<400> 183  
 Glu Leu Tyr Leu Asp Gly Asn Gln Phe Thr Leu Val Pro Lys Glu Leu  
 1 5 10 15  
 Ser Asn Tyr Lys His Leu Thr Leu Ile Asp Leu Ser Asn Asn Arg Ile  
 20 25 30  
 Ser Thr Leu Ser Asn Gln Ser Phe Ser Asn Met Thr Gln Leu Leu Thr  
 35 40 45  
 Leu Ile Leu Ser Tyr Asn Arg Leu Arg Cys Ile Pro Pro Arg Thr Phe  
 50 55 60  
 Asp Gly Leu Lys Ser Leu Arg Leu Leu Ser Leu His Gly Asn Asp Ile  
 65 70 75 80  
 Ser Val Val Pro Glu Gly Ala Phe Gly Asp Leu Ser Ala Leu Ser His  
 85 90 95  
 Leu Ala Ile Gly Ala Asn Pro Leu Tyr Cys Asp Cys Asn Met Gln Trp  
 100 105 110  
 Leu Ser Asp Trp Val Lys Ser Glu Tyr Lys Glu Pro Gly Ile Ala Arg  
 115 120 125  
 Cys Ala Gly Pro Gly Glu Met Ala Asp Lys Leu Leu Leu Thr Thr Pro  
 130 135 140  
 Ser Lys Asn Phe Thr Cys Gln Gly Pro Val Asp Val Thr Ile Gln Ala  
 145 150 155 160  
 Lys Cys Asn Pro Cys Leu Ser Asn Pro Cys Lys Asn Asp Gly Thr Cys  
 165 170 175  
 Asn Asn Asp Pro Val Asp Phe Tyr Arg Cys Thr Cys Pro Tyr Gly Phe  
 180 185 190  
 Lys Gly Gln Asp Cys Asp Val Pro Ile His Ala Cys Thr Ser Asn Pro  
 195 200 205  
 Cys Lys His Gly Gly Thr Cys His Leu Lys Pro Arg Arg Glu Thr Trp  
 210 215 220  
 Ile Trp Cys Thr Cys Ala Asp Gly Phe Glu Gly Glu Ser Cys Asp Ile  
 225 230 235 240  
 Asn Ile Asp Asp Cys Glu Asp Asn Asp Cys Glu Asn Asn Ser Thr Cys  
 245 250 255

Val Asp Gly Ile Asn Asn Tyr Thr Cys Leu Cys Pro Pro Glu Tyr Thr  
 260 265 270  
 Gly Glu Leu Cys Glu Glu Lys Leu Asp Phe Cys Ala Gln Asp Leu Asn  
 275 280 285  
 Pro Cys Gln His Asp Ser Lys Cys Ile Leu Thr Pro Lys Gly Phe Lys  
 290 295 300  
 Cys Asp Cys Thr Pro Gly Tyr Ile Gly Glu His Cys Asp Ile Asp Phe  
 305 310 315 320  
 Asp Asp Cys Gln Asp Asn Lys Cys Lys Asn Gly Ala His Cys Thr Asp  
 325 330 335  
 Ala Val Asn Gly Tyr Thr Cys Val Cys Pro Glu Gly Tyr Ser Gly Leu  
 340 345 350  
 Phe Cys Glu Phe Ser Pro Pro Met Val Phe Leu Arg Thr Ser Pro Cys  
 355 360 365  
 Asp Asn Phe Asp Cys Gln Asn Gly Ala Gln Cys Ile Ile Arg Val Asn  
 370 375 380  
 Glu Pro Ile Cys Gln Cys Leu Pro Gly Tyr Leu Gly Glu Lys Cys Glu  
 385 390 395 400  
 Lys Leu Val Ser Val Ser Ile Leu Val Asn Lys Glu Ser Tyr Leu Gln  
 405 410 415  
 Ile Pro Ser Ala Lys Val Arg Pro Gln Thr Asn Ile Thr Leu Gln Ile  
 420 425 430  
 Ala Thr Asp Glu Asp Ser Gly Ile Leu Leu Tyr Lys Gly Asp Lys Asp  
 435 440 445  
 His Ile Ala Val Glu Ser Ile Glu Gly Ile Arg Ala Ser Tyr Asp Thr  
 450 455 460  
 Gly Ser His Pro Ala Ser Ala Ile Tyr Ser Val Glu Thr Ile Asn Asp  
 465 470 475 480  
 Gly Asn Phe His Ile Val Glu Leu Leu Thr Leu Asp Ser Ser Leu Ser  
 485 490 495  
 Leu Ser Val Asp Gly Gly Ser Pro Lys Ile Ile Thr Asn Leu Ser Lys  
 500 505 510  
 Gln Ser Thr Leu Asn Phe Asp Ser Pro Leu Tyr Val Gly Gly Met Pro  
 515 520 525  
 Gly Lys Asn Asn Val Ala Ser Leu Arg Gln Ala Pro Gly Gln Asn Gly  
 530 535 540  
 Thr Ser Phe His Gly Cys Ile Arg Asn Leu Tyr Ile Asn Ser Glu Leu  
 545 550 555 560  
 Gln Asp Phe Arg Lys Val Pro Met Gln Thr Gly Ile Leu Pro Gly Cys  
 565 570 575  
 Glu Pro Cys His Lys Lys Val Cys Ala His Gly Thr Cys Gln Pro Ser  
 580 585 590  
 Ser Gln Ser Gly Phe Thr Cys Glu Cys Glu Glu Gly Trp Met Gly Pro  
 595 600 605  
 Leu Cys Asp Gln Arg Thr Asn Asp Pro Cys Leu Gly Asn Lys Cys Val  
 610 615 620  
 His Gly Thr Cys Leu Pro Ile Asn Ala Phe Ser Tyr Ser Cys Lys Cys  
 625 630 635 640  
 Leu Glu Gly His Gly Gly Val Leu Cys Asp Glu Glu Glu Asp Leu Phe  
 645 650 655  
 Asn Pro Leu Pro Gly Asp Gln Val Gln Ala Arg Glu Val Gln Ala Leu  
 660 665 670  
 Trp Ala Arg Ala Ala Leu Leu Trp Met Gln Gln Trp Ile His Arg Gly  
 675 680 685  
 Gln Leu Thr Gln Arg Ile Ser Cys Arg Gly Glu Arg Ile Arg Asp Tyr  
 690 695 700  
 Tyr Gln Ser Ser Arg Val Arg Cys Leu Ser Asn Asp

&lt;210&gt; 184

&lt;211&gt; 340

&lt;212&gt; PRT

&lt;213&gt; mouse

&lt;400&gt; 184

Asp Gly Ser Leu Trp Leu Gln Ala Thr Gln Pro Asp Asp Ala Gly His  
 1 5 10 15  
 Tyr Thr Cys Val Pro Ser Asn Gly Phe Leu His Pro Pro Ser Ala Ser  
 20 25 30  
 Ala Tyr Leu Thr Val Leu Tyr Pro Ala Gln Val Thr Val Met Pro Pro  
 35 40 45  
 Glu Thr Pro Leu Pro Thr Gly Met Arg Gly Val Ile Arg Cys Pro Val  
 50 55 60  
 Arg Ala Asn Pro Pro Leu Leu Phe Val Thr Trp Thr Lys Asp Gly Gln  
 65 70 75 80  
 Ala Leu Gln Leu Asp Lys Phe Pro Gly Trp Ser Leu Gly Pro Glu Gly  
 85 90 95  
 Ser Leu Ile Ile Ala Leu Gly Asn Glu Asp Ala Leu Gly Glu Tyr Ser  
 100 105 110  
 Cys Thr Pro Tyr Asn Ser Leu Gly Thr Ala Gly Pro Ser Pro Val Thr  
 115 120 125  
 Arg Val Leu Leu Lys Ala Pro Pro Ala Phe Ile Asp Gln Pro Lys Glu  
 130 135 140  
 Glu Tyr Phe Gln Glu Val Gly Arg Glu Leu Leu Ile Pro Cys Ser Ala  
 145 150 155 160  
 Arg Gly Asp Pro Pro Pro Ile Val Ser Trp Ala Lys Val Gly Arg Gly  
 165 170 175  
 Leu Gln Gly Gln Ala Gln Val Asp Ser Asn Asn Ser Leu Val Leu Arg  
 180 185 190  
 Pro Leu Thr Lys Glu Ala Gln Gly Arg Trp Glu Cys Ser Ala Ser Asn  
 195 200 205  
 Ala Val Ala Arg Val Thr Thr Ser Thr Asn Val Tyr Val Leu Gly Thr  
 210 215 220  
 Ser Pro His Val Val Thr Asn Val Ser Val Val Pro Leu Pro Lys Gly  
 225 230 235 240  
 Ala Asn Val Ser Trp Glu Pro Gly Phe Asp Gly Gly Tyr Leu Gln Arg  
 245 250 255  
 Phe Ser Val Trp Tyr Thr Pro Leu Ala Lys Arg Pro Asp Arg Ala His  
 260 265 270  
 His Asp Trp Val Ser Leu Ala Val Pro Ile Gly Ala Thr His Leu Leu  
 275 280 285  
 Val Pro Gly Leu Gln Ala His Ala Gln Tyr Gln Phe Ser Val Leu Ala  
 290 295 300  
 Gln Asn Lys Leu Gly Ser Gly Pro Phe Ser Glu Ile Val Leu Ser Ile  
 305 310 315 320  
 Pro Glu Gly Leu Pro Thr Thr Pro Ala Ala Pro Gly Leu Pro Ala Thr  
 325 330 335  
 Arg Ser Arg Val  
 340

&lt;210&gt; 185

&lt;211&gt; 536

&lt;212&gt; PRT

&lt;213&gt; mouse

&lt;400&gt; 185

Lys Val Glu Gly Glu Gly Arg Gly Arg Trp Ala Leu Gly Leu Leu Arg  
 1 5 10 15  
 Thr Phe Asp Ala Gly Glu Phe Ala Gly Trp Glu Lys Val Gly Ser Gly  
 20 25 30  
 Gly Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp  
 35 40 45  
 Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg

50	55	60
Met Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg		
65	70	75
Tyr Ile Leu Pro Val Tyr Gly Ile Cys Gln Glu Pro Val Gly Leu Val		80
	85	90
Met Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu		95
	100	105
Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val		110
	115	120
Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp		125
	130	135
Leu Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr Gln Met Ser Arg		140
145	150	155
Phe Leu Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His		160
	165	170
Asp Leu Ser Met Asp Gly Leu Phe Gly Thr Ile Gly Tyr Leu Pro Pro		175
	180	185
Glu Arg Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val		190
	195	200
Tyr Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Asn Asn Pro		205
	210	215
Phe Ala Asp Glu Lys Asn Ile Leu His Ile Met Met Lys Val Val Lys		220
225	230	235
Gly His Arg Pro Glu Leu Pro Pro Ile Cys Arg Pro Arg Pro Arg Ala		240
	245	250
Cys Ala Ser Leu Ile Gly Leu Met Gln Arg Cys Trp His Ala Asp Pro		255
	260	265
Gln Val Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu		270
	275	280
Cys Glu Lys Pro Asp Glu Glu Val Lys Asp Leu Ala His Glu Pro Gly		285
	290	295
Glu Lys Ser Ser Leu Glu Ser Lys Ser Glu Ala Arg Pro Glu Ser Ser		300
305	310	315
Arg Leu Lys Arg Ala Ser Ala Pro Pro Phe Asp Asn Asp Cys Ser Leu		320
	325	330
Ser Glu Leu Leu Ser Gln Leu Asp Ser Gly Ile Phe Pro Arg Leu Leu		335
	340	345
Lys Gly Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Cys Lys Leu Pro		350
	355	360
Ser Ser Ser Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser		365
	370	375
Ala Phe Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg Glu Ala		380
385	390	395
Ser Thr Gly Asp Leu Gly Pro Thr Asp Ile Gln Lys Lys Lys Leu Val		400
	405	410
Asp Ala Ile Ile Ser Gly Asp Thr Ser Arg Leu Met Lys Ile Leu Gln		415
	420	425
Pro Gln Asp Val Asp Leu Val Leu Asp Ser Ser Ala Ser Leu Leu His		430
	435	440
Leu Ala Val Glu Ala Gly Gln Glu Glu Cys Val Lys Trp Leu Leu Leu		445
	450	455
Asn Asn Ala Asn Pro Asn Leu Thr Asn Arg Lys Gly Ser Thr Pro Leu		460
465	470	475
His Met Ala Val Glu Arg Lys Gly Arg Gly Ile Val Glu Leu Leu Leu		480
	485	490
Ala Arg Lys Thr Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Ala		495
	500	505
Leu His Phe Ala Ala Gln Asn Gly Asp Glu Gly Gln His Lys Ala Ala		510
	515	520
Ala Arg Glu Glu Cys Phe Cys Gln		525
530	535	

<210> 186  
 <211> 337  
 <212> PRT  
 <213> Rat

<220>

<400> 186  
 Arg Phe Gly Tyr Gln Met Asp Glu Gly Asn Gln Cys Val Asp  
 1 5 10 15  
 Val Asp Glu Cys Ala Thr Asp Ser His Gln Cys Asn Pro Thr Gln Ile  
 20 25 30  
 Cys Ile Asn Thr Glu Gly Gly Tyr Thr Cys Ser Cys Thr Asp Gly Tyr  
 35 40 45  
 Trp Leu Leu Glu Gly Gln Cys Leu Asp Ile Asp Glu Cys Arg Tyr Gly  
 50 55 60  
 Tyr Cys Gln Gln Leu Cys Ala Asn Val Pro Gly Ser Tyr Ser Cys Thr  
 65 70 75 80  
 Cys Asn Pro Gly Phe Thr Leu Asn Asp Asp Gly Arg Ser Cys Gln Asp  
 85 90 95  
 Val Asn Glu Cys Glu Thr Glu Asn Pro Cys Val Gln Thr Cys Val Asn  
 100 105 110  
 Thr Tyr Gly Ser Phe Ile Cys Arg Cys Asp Pro Gly Tyr Glu Leu Glu  
 115 120 125  
 Glu Asp Gly Ile His Cys Ser Asp Met Asp Glu Cys Ser Phe Ser Glu  
 130 135 140  
 Phe Leu Cys Gln His Glu Cys Val Asn Gln Pro Gly Ser Tyr Phe Cys  
 145 150 155 160  
 Ser Cys Pro Pro Gly Tyr Val Leu Leu Glu Asp Asn Arg Ser Cys Gln  
 165 170 175  
 Asp Ile Asn Glu Cys Glu His Arg Asn His Thr Cys Thr Pro Leu Gln  
 180 185 190  
 Thr Cys Tyr Asn Leu Gln Gly Gly Phe Lys Cys Ile Asp Pro Ile Val  
 195 200 205  
 Cys Glu Glu Pro Tyr Leu Leu Ile Gly Asp Asn Arg Cys Met Cys Pro  
 210 215 220  
 Ala Glu Asn Thr Gly Cys Arg Asp Gln Pro Phe Thr Ile Leu Phe Arg  
 225 230 235 240  
 Asp Met Asp Val Val Ser Gly Arg Ser Val Pro Ala Asp Ile Phe Gln  
 245 250 255  
 Met Gln Ala Thr Thr Arg Tyr Pro Gly Ala Tyr Tyr Ile Phe Gln Ile  
 260 265 270  
 Lys Ser Gly Asn Glu Gly Arg Glu Phe Tyr Met Arg Gln Thr Gly Pro  
 275 280 285  
 Ile Ser Ala Thr Leu Val Met Thr Arg Pro Ile Lys Gly Pro Arg Asp  
 290 295 300  
 Ile Gln Leu Asp Leu Glu Met Ile Thr Val Asn Thr Val Ile Asn Phe  
 305 310 315 320  
 Arg Gly Ser Ser Val Ile Arg Leu Arg Ile Tyr Val Ser Gln Tyr Pro  
 325 330 335  
 Phe

<210> 187  
 <211> 152  
 <212> PRT  
 <213> mouse

<400> 187

Met Ala Leu Gly Val Leu Ile Ala Val Cys Leu Leu Phe Lys Ala Met  
 1 5 10 15  
 Lys Ala Ala Leu Ser Glu Glu Ala Glu Val Ile Pro Pro Ser Thr Ala  
 20 25 30  
 Gln Gln Ser Asn Trp Thr Phe Asn Asn Thr Glu Ala Asp Tyr Ile Glu  
 35 40 45  
 Glu Pro Val Ala Leu Lys Phe Ser His Pro Cys Leu Glu Asp His Asn  
 50 55 60  
 Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Lys Gln  
 65 70 75 80  
 Ala Ile Cys Arg Cys Phe Thr Gly Tyr Thr Gly Gln Arg Cys Glu His  
 85 90 95  
 Leu Thr Leu Thr Ser Tyr Ala Val Asp Ser Tyr Glu Lys Tyr Ile Ala  
 100 105 110  
 Ile Gly Ile Gly Val Gly Leu Leu Ile Ser Ala Phe Leu Ala Val Phe  
 115 120 125  
 Tyr Cys Tyr Ile Arg Lys Arg Cys Ile Asn Leu Lys Ser Pro Tyr Ile  
 130 135 140  
 Ile Cys Ser Gly Gly Ser Pro Leu  
 145 150

&lt;210&gt; 188

&lt;211&gt; 118

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;220&gt;

&lt;400&gt; 188

Leu Val Pro Gln Phe Gly Thr Arg Ile Arg Tyr ThrAla Tyr Asp Arg  
 1 5 10 15  
 Ala Tyr Asn Arg Ala Ser Cys Lys Phe Ile Val Lys Val Gln Val Arg  
 20 25 30  
 Arg Cys Pro Ile Leu Lys Pro Pro Gln His Gly Tyr Leu Thr Cys Ser  
 35 40 45  
 Ser Ala Gly Asp Asn Tyr Gly Ala Ile Cys Glu Tyr His Cys Asp Gly  
 50 55 60  
 Gly Tyr Glu Arg Gln Gly Thr Pro Ser Arg Val Cys Gln Ser Ser Arg  
 65 70 75 80  
 Gln Trp Ser Gly Ser Pro Pro Val Cys Thr Pro Met Lys Ile Asn Val  
 85 90 95  
 Asn Val Asn Ser Ala Ala Gly Leu Leu Asp Gln Phe Tyr Glu Lys Gln  
 100 105 110  
 Arg Leu Leu Ile Val Ser  
 115

&lt;210&gt; 189

&lt;211&gt; 299

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;220&gt;

&lt;400&gt; 189

Met Gly Thr Lys Ala Gln Val Glu Arg Lys Leu Leu Cys Leu Phe Ile  
 1 5 10 15  
 Leu Ala Ile Leu Leu Cys Ser Leu Ala Leu Gly Ser Val Thr Val His  
 20 25 30  
 Ser Ser Glu Pro Glu Val Arg Ile Pro Glu Asn Asn Pro Val Lys Leu  
 35 40 45  
 Ser Cys Ala Tyr Ser Gly Phe Ser Ser Pro Arg Val Glu Trp Lys Phe

50                      55                      60  
 Asp Gln Gly Asp Thr Thr Arg Leu Val Cys Tyr Asn Asn Lys Ile Thr  
 65                      70                      75                      80  
 Ala Ser Tyr Glu Asp Arg Val Thr Phe Leu Pro Thr Gly Ile Thr Phe  
                     85                      90                      95  
 Lys Ser Val Thr Arg Glu Asp Thr Gly Thr Tyr Thr Cys Met Val Ser  
                     100                      105                      110  
 Glu Glu Gly Gly Asn Ser Tyr Gly Glu Val Lys Val Lys Leu Ile Val  
                     115                      120                      125  
 Leu Val Pro Pro Ser Lys Pro Thr Val Asn Ile Pro Ser Ser Ala Thr  
                     130                      135                      140  
 Ile Gly Asn Arg Ala Val Leu Thr Cys Ser Glu Gln Asp Gly Ser Pro  
 145                      150                      155                      160  
 Pro Ser Glu Tyr Thr Trp Phe Lys Asp Gly Ile Val Met Pro Thr Asn  
                     165                      170                      175  
 Pro Lys Ser Thr Arg Ala Phe Ser Asn Ser Ser Tyr Val Leu Asn Pro  
                     180                      185                      190  
 Thr Thr Gly Glu Leu Val Phe Asp Pro Leu Ser Ala Ser Asp Thr Gly  
                     195                      200                      205  
 Glu Tyr Ser Cys Glu Ala Arg Asn Gly Tyr Gly Thr Pro Met Thr Ser  
                     210                      215                      220  
 Asn Ala Val Arg Met Glu Ala Val Glu Arg Asn Val Gly Val Ile Val  
 225                      230                      235                      240  
 Ala Ala Val Leu Val Thr Leu Ile Leu Leu Gly Ile Leu Val Phe Gly  
                     245                      250                      255  
 Ile Trp Phe Ala Tyr Ser Arg Gly His Phe Asp Arg Thr Lys Lys Gly  
                     260                      265                      270  
 Thr Ser Ser Lys Lys Val Ile Tyr Ser Gln Pro Ser Ala Arg Ser Glu  
                     275                      280                      285  
 Gly Glu Phe Lys Gln Thr Ser Ser Phe Leu Val  
                     290                      295

<210> 190  
 <211> 91  
 <212> PRT  
 <213> Human

<400> 190  
 Gln Pro Thr Val Phe Trp Pro Lys Thr Ser Ala Lys Lys Gly Asn Trp  
 1                      5                      10                      15  
 Val Leu Arg Leu Gly Leu Ser Asn Pro Asp Arg Pro Ala Arg Gln Asn  
                     20                      25                      30  
 Asn Trp Phe Leu Pro Ala Ser Arg Glu Ile Pro Glu His Ser Ala Leu  
                     35                      40                      45  
 Thr Arg Tyr Pro Ala Gln Ile Arg Gly Cys Trp Pro His Arg Leu Thr  
                     50                      55                      60  
 Lys Pro Gln Thr Cys Leu Pro Gln Ala Arg Ser Tyr Leu Ser His Glu  
 65                      70                      75                      80  
 Val Thr Gln Ala Thr Arg Thr Cys Pro Gly Gly  
                     85                      90

<210> 191  
 <211> 89  
 <212> PRT  
 <213> mouse

<400> 191  
 Gly Ala Trp Ala Met Leu Tyr Gly Val Ser Met Leu Cys Val Leu Asp  
 1                      5                      10                      15  
 Leu Gly Gln Pro Ser Val Val Glu Glu Pro Gly Cys Gly Pro Gly Lys  
                     20                      25                      30

Val Gln Asn Gly Ser Gly Asn Asn Thr Arg Cys Cys Ser Leu Tyr Ala  
           35                                  40                                  45  
 Pro Gly Lys Glu Asp Cys Pro Lys Glu Arg Cys Ile Cys Val Thr Pro  
           50                                  55                                  60  
 Glu Tyr His Cys Gly Asp Pro Gln Cys Lys Ile Cys Lys His Tyr Pro  
 65                                  70                                  75                                  80  
 Cys Gln Pro Gly Gln Arg Val Glu Val  
                                   85

<210> 192  
 <211> 299  
 <212> PRT  
 <213> mouse

<220>

<400> 192  
 Ala Arg Ala Gly Ala Cys Tyr Cys Pro Ala Gly Phe Leu Gly Ala Asp  
 1                                  5                                  10                                  15  
 Cys Ser Leu Ala Cys Pro Gln Gly Arg Phe Gly Pro Ser Cys Ala His  
                                   20                                  25                                  30  
 Val Cys Thr Cys Gly Gln Gly Ala Ala Cys Asp Pro Val Ser Gly Thr  
                                   35                                  40                                  45  
 Cys Ile Cys Pro Pro Gly Lys Thr Gly Gly His Cys Glu Arg Gly Cys  
                                   50                                  55                                  60  
 Pro Gln Asp Arg Phe Gly Lys Gly Cys Glu His Lys Cys Ala Cys Arg  
 65                                  70                                  75                                  80  
 Asn Gly Gly Leu Cys His Ala Thr Asn Gly Ser Cys Ser Cys Pro Leu  
                                   85                                  90                                  95  
 Gly Trp Met Gly Pro His Cys Glu His Ala Cys Pro Ala Gly Arg Tyr  
                                   100                                  105                                  110  
 Gly Ala Ala Cys Leu Leu Glu Cys Ser Cys Gln Asn Asn Gly Ser Cys  
                                   115                                  120                                  125  
 Glu Pro Thr Ser Gly Ala Cys Leu Cys Gly Pro Gly Phe Tyr Gly Gln  
                                   130                                  135                                  140  
 Ala Cys Glu Asp Thr Cys Pro Ala Gly Phe His Gly Ser Gly Cys Gln  
 145                                  150                                  155                                  160  
 Arg Val Cys Glu Cys Gln Gln Gly Ala Pro Cys Asp Pro Val Ser Gly  
                                   165                                  170                                  175  
 Arg Cys Leu Cys Pro Ala Gly Phe Arg Gly Gln Phe Cys Glu Arg Gly  
                                   180                                  185                                  190  
 Cys Lys Pro Gly Phe Phe Gly Asp Gly Cys Leu Gln Gln Cys Asn Cys  
                                   195                                  200                                  205  
 Pro Thr Gly Val Pro Cys Asp Pro Ile Ser Gly Leu Cys Leu Cys Pro  
                                   210                                  215                                  220  
 Pro Gly Arg Ala Gly Thr Thr Cys Asp Leu Asp Cys Arg Arg Gly Arg  
 225                                  230                                  235                                  240  
 Phe Gly Pro Gly Cys Ala Leu Arg Cys Asp Cys Gly Gly Gly Ala Asp  
                                   245                                  250                                  255  
 Cys Asp Pro Ile Ser Gly Gln Cys His Cys Val Asp Ser Tyr Thr Gly  
                                   260                                  265                                  270  
 Pro Thr Cys Arg Glu Val Pro Thr Gln Leu Ser Ser Ile Arg Pro Ala  
                                   275                                  280                                  285  
 Pro Gln His Ser Ser Ser Lys Ala Met Lys His  
                                   290                                  295

<210> 193  
 <211> 314  
 <212> PRT  
 <213> mouse



&lt;220&gt;

&lt;400&gt; 193

Glu Glu Pro Cys Asn Asn Gly Ser Glu Ile Leu Ala Tyr Asn Ile Asp  
 1 5 10 15  
 Leu Gly Asp Ser Cys Ile Thr Val Gly Asn Thr Thr Thr His Val Met  
 20 25 30  
 Lys Asn Leu Leu Pro Glu Thr Thr Tyr Arg Ile Arg Ile Gln Ala Ile  
 35 40 45  
 Asn Glu Ile Gly Val Gly Pro Phe Ser Gln Phe Ile Lys Ala Lys Thr  
 50 55 60  
 Arg Pro Leu Pro Pro Ser Pro Pro Arg Leu Glu Cys Ala Ala Ser Gly  
 65 70 75 80  
 Pro Gln Ser Leu Lys Leu Lys Trp Gly Asp Ser Asn Ser Lys Thr His  
 85 90 95  
 Ala Ala Gly Asp Met Val Tyr Thr Leu Gln Leu Glu Asp Arg Asn Lys  
 100 105 110  
 Arg Phe Ile Ser Ile Tyr Arg Gly Pro Ser His Thr Tyr Lys Val Gln  
 115 120 125  
 Arg Leu Thr Glu Phe Thr Cys Tyr Ser Phe Arg Ile Gln Ala Met Ser  
 130 135 140  
 Glu Ala Gly Glu Gly Pro Tyr Ser Glu Thr Tyr Thr Phe Ser Thr Thr  
 145 150 155 160  
 Lys Ser Val Pro Pro Thr Leu Lys Ala Pro Arg Val Thr Gln Leu Glu  
 165 170 175  
 Gly Asn Ser Cys Glu Ile Phe Trp Glu Thr Val Pro Pro Met Arg Gly  
 180 185 190  
 Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp Ser Glu  
 195 200 205  
 Tyr Lys Gln Val Tyr Lys Gly Glu Glu Ala Thr Phe Gln Ile Ser Gly  
 210 215 220  
 Leu Gln Ser Asn Thr Asp Tyr Arg Phe Arg Val Cys Ala Cys Arg Arg  
 225 230 235 240  
 Cys Val Asp Thr SerGln Glu Leu Ser Gly Ala Phe Ser Pro Ser Ala  
 245 250 255  
 Ala Phe Met Leu Gln Gln Arg Glu Val Met Leu Thr Gly Asp Leu Gly  
 260 265 270  
 Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp Glu Gln  
 275 280 285  
 Phe Ala Ala Leu Ile Val Leu Gly Phe Ala Thr Leu Ser Ile Leu Phe  
 290 295 300  
 Ala Phe Ile Leu Gln Tyr Phe Leu Met Lys  
 305 310

&lt;210&gt; 194

&lt;211&gt; 109

&lt;212&gt; PRT

&lt;213&gt; mouse

&lt;400&gt; 194

Gly Thr Arg Val Gly Thr Pro Tyr Tyr Met Ser Pro Glu Arg Ile His  
 1 5 10 15  
 Glu Asn Gly Tyr Asn Phe Lys Ser Asp Ile Trp Ser Leu Gly Cys Leu  
 20 25 30  
 Leu Tyr Glu Met Ala Ala Leu Gln Ser Pro Phe Tyr Gly Asp Lys Met  
 35 40 45  
 Asn Leu Tyr Ser Leu Cys Lys Lys Ile Glu Gln Cys Asp Tyr Pro Pro  
 50 55 60  
 Leu Pro Ser Asp His Tyr Ser Glu Glu Leu Arg Gln Leu Val Asn Ile  
 65 70 75 80  
 Cys Ile Asn Pro Asp Pro Glu Lys Arg Pro Asp Ile Ala Tyr Val Tyr

85 90 95  
 Asp Val Ala Lys Arg Met His Ala Cys Thr Ala Ser Thr  
 100 105

<210> 195  
 <211> 237  
 <212> PRT  
 <213> mouse

<400> 195  
 Met Leu Ser Leu Arg Ser Leu Leu Pro His Leu Gly Leu Phe Leu Cys  
 1 5 10 15  
 Leu Ala Leu His Leu Ser Pro Ser Leu Ser Ala Ser Asp Asn Gly Ser  
 20 25 30  
 Cys Val Val Leu Asp Asn Ile Tyr Thr Ser Asp Ile Leu Glu Ile Ser  
 35 40 45  
 Thr Met Ala Asn Val Ser Gly Gly Asp Val Thr Tyr Thr Val Thr Val  
 50 55 60  
 Pro Val Asn Asp Ser Val Ser Ala Val Ile Leu Lys Ala Val Lys Glu  
 65 70 75 80  
 Asp Asp Ser Pro Val Gly Thr Trp Ser Gly Thr Tyr Glu Lys Cys Asn  
 85 90 95  
 Asp Ser Ser Val Tyr Tyr Asn Leu Thr Ser Gln Ser Gln Ser Val Phe  
 100 105 110  
 Gln Thr Asn Trp Thr Val Pro Thr Ser Glu Asp Val Thr Lys Val Asn  
 115 120 125  
 Leu Gln Val Leu Ile Val Val Asn Arg Thr Ala Ser Lys Ser Ser Val  
 130 135 140  
 I, s Met Glu Gln Val Gln Pro Ser Ala Ser Thr Pro Ile Pro Glu Ser  
 145 150 155 160  
 Ser Glu Thr Ser Gln Thr Ile Asn Thr Thr Pro Thr Val Asn Thr Ala  
 165 170 175  
 Lys Thr Thr Ala Lys Asp Thr Ala Asn Thr Thr Ala Val Thr Thr Ala  
 180 185 190  
 Asn Thr Thr Ala Asn Thr Thr Ala Val Thr Thr Ala Lys Thr Thr Ala  
 195 200 205  
 Lys Ser Leu Ala Ile Arg Thr Leu Gly Ser Pro Leu Ala Gly Ala Leu  
 210 215 220  
 His Ile Leu Leu Val Phe Leu Ile Ser Lys Leu Leu Phe  
 225 230 235

<210> 196  
 <211> 154  
 <212> PRT  
 <213> Human

<400> 196  
 Met Ala Leu Gly Val Pro Ile Ser Val Tyr Leu Leu Phe Asn Ala Met  
 1 5 10 15  
 Thr Ala Leu Thr Glu Glu Ala Ala Val Thr Val Thr Pro Pro Ile Thr  
 20 25 30  
 Ala Gln Gln Gly Asn Trp Thr Val Asn Lys Thr Glu Ala His Asn Ile  
 35 40 45  
 Glu Gly Pro Ile Ala Leu Lys Phe Ser His Leu Cys Leu Glu Asp His  
 50 55 60  
 Asn Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Glu  
 65 70 75 80  
 Lys Ala Ile Cys Arg Cys Phe Thr Gly Tyr Thr Gly Glu Arg Cys Glu  
 85 90 95  
 His Leu Thr Leu Thr Ser Tyr Ala Val Asp Ser Tyr Glu Lys Tyr Ile  
 100 105 110

Ala Ile Gly Ile Gly Val Gly Leu Leu Leu Ser Gly Phe Leu Val Ile  
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 Phe Tyr Cys Tyr Ile Arg Lys Arg Cys Leu Lys Leu Lys Ser Pro Tyr  
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 Asn Val Cys Ser Gly Glu Arg Arg Pro Leu  
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 <212> PRT  
 <213> Rat

<400> 197  
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 Met Pro Arg Pro Ala Glu Arg Gly Pro Pro Val Arg Leu Phe Thr Glu  
 35 40 45  
 Glu Glu Leu Ala Arg Tyr Ser Gly Glu Glu Glu Asp Gln Pro Ile Tyr  
 50 55 60  
 Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu Phe  
 65 70 75 80  
 Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Ala Gly Lys Asp Ser Ser  
 85 90 95  
 Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His Asp  
 100 105 110  
 Ile Ser Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Asp Ile Phe  
 115 120 125  
 Ser Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala Arg  
 130 135 140  
 Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro Glu  
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 Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe  
 165 170

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 <211> 1399  
 <212> DNA  
 <213> Mouse

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&lt;210&gt; 199

&lt;211&gt; 469

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 199

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&lt;210&gt; 200

&lt;211&gt; 529

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 200

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&lt;210&gt; 201

&lt;211&gt; 1230

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 201

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&lt;210&gt; 202

&lt;211&gt; 778

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 202

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&lt;210&gt; 203

&lt;211&gt; 1123

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 203

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&lt;210&gt; 204

&lt;211&gt; 434

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 204

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 <211> 783  
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<400> 205

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 <212> DNA  
 <213> Mouse

<400> 206

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<210> 207  
 <211> 501  
 <212> DNA  
 <213> Mouse

<400> 207

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&lt;210&gt; 209

&lt;211&gt; 962

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 209

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aa						962

&lt;210&gt; 210

&lt;211&gt; 778

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 210

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&lt;210&gt; 211

&lt;211&gt; 1152

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 211

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&lt;210&gt; 212

&lt;211&gt; 446

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 212

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&lt;210&gt; 213

&lt;211&gt; 2728

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 213

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&lt;210&gt; 214

&lt;211&gt; 2046

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 214

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 <213> Mouse

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 <212> DNA  
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<400> 218

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 <212> DNA  
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&lt;211&gt; 376

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 220

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ccctcagctc	tggcgacggc	gcttgacgtg	ggcttgcca	actggagctt	cctgtatgtc	240
accgtctcgc	tgtgagtact	ggccatgccc	tgctgctccc	cttcaggtg	aagctgtctg	300
ccctcagc	ggggtgtctg	cacaccgggc	tgctaggcca	gccactccac	cactctggga	360
ccagcccttg	ctctct					376

&lt;210&gt; 221

&lt;211&gt; 433

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 221

agcttcttct	cagagcaaac	agtaagcaac	agaaaatata	catttgatga	aacattcttt	60
gcattagaga	aacatgaaaa	taaatataat	tcaaggaagt	ataatgattc	tctaatatgt	120
ctttctcaga	cctgtactag	tttaccggtt	caagaagctc	tcatacatt	tttcacttgt	180
attttacata	ttgctattcg	ggtaattcaa	ataaaatgca	ggtcttgtaa	aagaataaaa	240
acattgacaa	gtatgcatgt	gccagggacc	aaattagagg	gttctttggg	gcagttagtc	300
caaattctca	gatttgaagg	ataatatgta	ccaataaaaa	aaaaatctgc	tgctagacat	360
ttacagcagt	gctctgtctt	gcttcacatt	agaaatcgaa	aacagctgtt	ctcaacaagc	420
caattttatt	ttt					433

&lt;210&gt; 222

&lt;211&gt; 530

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 222

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atattgactt	tgtaagaagt	atactcttgg	aaataggtgc	taagcaaata	gtgtttggga	180
cctctaagct	tatgtgaccg	gagttttact	cttttgctct	taattttctc	attttctttt	240
gactgggtgaa	aagttagcag	gtaagttaga	atltggctcg	aagcctgctt	ccttagttga	300
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&lt;210&gt; 223

&lt;211&gt; 550

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 223

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ctccttgctg	ggacagagt	gtgaagacgt	attcctcacc	tccttgccct	tcagtaaatg	300
gccacgatgt	gactatttgt	tgagggttcc	agcctcttcc	aagaccttgc	caggctgagt	360
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tccttgcccc						550

&lt;210&gt; 224

&lt;211&gt; 470

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 224

aggcctgttc	accaccactc	ctgttctccg	ctaagctttt	ctttggcttt	tggtgggttg	60
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taccttctgt	cagcagctct	ttccctgtct	gtatagcaac	ccttctaccc	ttgcttttct	300
tgcttctctc	tcttctactc	accttaagca	gagttcaaag	actcaacttc	aacattgggtc	360
atctgggtgt	gtattttatat	gtgaataatg	atatcagatc	cagagtaaca	cctttgctgt	420
cttcttagga	tgggtgagtg	cacggggctc	gggctctttg	ctgaataactt		470

&lt;210&gt; 225

&lt;211&gt; 1752

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 225

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ggagcaagtt	cacacagatc	tcaccagtct	ggttgcagct	gaagagacgt	ggtcggggaga	420
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ggagctagcc	ag					1752

&lt;210&gt; 226

&lt;211&gt; 2165

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 226

ggcacgagcc	tgctgccctc	ttgcagacag	gaaagacatg	gtctctgcgc	ccggatccta	60
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tgtctcctgg	cctaccgtgt	ggataaacgt	tttctgtggc	ttcagtgggg	ctggttccct	240
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aaaaa						2165

&lt;210&gt; 227

&lt;211&gt; 1348

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (644) ... (644)

&lt;400&gt; 227

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gctcttttta	aaagtttgaa	aaaaaaaa				1380

&lt;210&gt; 228

&lt;211&gt; 2296

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (2255) ... (2255)

&lt;400&gt; 228

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aacactggaa	aagagactga	gagaagcaat	gtacntgtac	atttgccata	taatttatat	2280
ttaagaactt	tttatt					2296

&lt;210&gt; 229

&lt;211&gt; 1704

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;220&gt;

&lt;400&gt; 229

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&lt;210&gt; 230

&lt;211&gt; 2004

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 230

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&lt;210&gt; 231

&lt;211&gt; 1397

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 231

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&lt;210&gt; 232

&lt;211&gt; 861

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 232

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&lt;210&gt; 233

&lt;211&gt; 445

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 233

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&lt;210&gt; 234

&lt;211&gt; 565

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 234

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&lt;210&gt; 235

&lt;211&gt; 476

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 235

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&lt;210&gt; 236

&lt;211&gt; 607

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 236

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&lt;210&gt; 237

&lt;211&gt; 513

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 237

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&lt;210&gt; 238

&lt;211&gt; 944

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 238

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<211> 386

<212> DNA

<213> Rat

<400> 239

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<210> 240

<211> 228

<212> DNA

<213> Rat

<400> 240

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<211> 452

<212> DNA

<213> Human

<400> 241

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<210> 242

<211> 1311

<212> DNA

<213> Mouse

<400> 242

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&lt;210&gt; 243

&lt;211&gt; 399

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 243

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&lt;210&gt; 244

&lt;211&gt; 1421

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (1370) ... (1370)

&lt;221&gt; unsure

&lt;222&gt; (1395) ... (1395)

&lt;400&gt; 244

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&lt;210&gt; 248

&lt;211&gt; 1308

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 248

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&lt;211&gt; 1212

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 249

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&lt;400&gt; 254

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&lt;211&gt; 1464

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 255

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&lt;210&gt; 256

&lt;211&gt; 2411

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 256

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&lt;210&gt; 257

&lt;211&gt; 3516

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 257

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&lt;211&gt; 946

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 258

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&lt;211&gt; 1018

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 259

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&lt;210&gt; 260

&lt;211&gt; 2800

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 260

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&lt;210&gt; 261

&lt;211&gt; 1335

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 261

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 <211> 1816  
 <212> DNA  
 <213> Mouse

<400> 262  
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 gaagattctt aagagcatgg ataagaatgg cacgatgacc atcgactgga acgagtggag 480  
 ggactaccac ctccctgcacc ctgtggagaa catcccgag atcatcctgt actggaagca 540  
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 ccacgaaagg cttgtggcag gctccttggc cggagccatt gccagagta gcatctaccc 960  
 aatggagggt ctgaagaccc gaatggccct gcggaacaac ggacagtact ccggcatgct 1020  
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<210> 263  
 <211> 764  
 <212> DNA  
 <213> Mouse

<400> 263  
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 cgggcggcat cccccggccg ccgcacgcac aggcggcgcg cctccttgcc tccctgctcc 180  
 ccaccgcgcc cctccggcca gcatgaggct cctggcggcc gcgtgctcc tgcgtctct 240  
 ggcgtgtgct gcctcgcgcg tggacgggtc caagtgtatg tgttcccgga aggggcccga 300  
 gatccgctac agcgacgtga agaagctgga aatgaagcca aagtaccac actgagagga 360  
 gaagatggtt atcgctacca ccaagagcat gtccagggtac cggggccagg agcactgcct 420  
 gcaccttaag ctgcagagca ccaaagcgtt catcaagtgg tacaatgcct ggaacgagaa 480  
 gcgcagggtc tacgaagaat aggggtggacg atcatggaaa gaaaaactcc agggcagttg 540  
 agagacttca gcagaggact ttgcagatta aaataaaagc cctttctttc tcacaagcat 600  
 aagacaaaatt atatattgct atgaagctct tcttaccagg gtcagttttt acattttata 660  
 gctgtgtgtg aaaggcttcc agatgtgaga tccagctcgc ctgcgcacca gacttcatta 720  
 caagtggctt tttgctgggc ggttggcggg gggcgggggg acct 764

<210> 264  
 <211> 1697  
 <212> DNA

&lt;213&gt; Mouse

&lt;400&gt; 264

gcgcggcecg	ggggactcac	attccccggt	ccccctccg	ccccacgcg	ctgggccatg	60
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gagtcacccg	aagccccctcc	gcagtccttg	acacagctgt	ggctcttccg	cttcttgttg	180
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cggagaagaact	acctggagac	aggcaggggt	ctctgcttcc	ccctggtgaa	agcctgtgtg	300
tttggcaatg	agcccaaggc	tcctgatgag	gttctcctgg	ctccgcggac	agagacagcg	360
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gccacatcac	caggagagca	tttcacagac	tcccagtttc	tgggtgctgat	gaaccgtgtg	540
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cccatgtacc	ggtactcctt	tgccagtctg	tcaaatgtgc	ttagcagctg	gtgccagtat	660
gaagcactta	agttcgtcag	cttccttacc	caggtgctgg	cgaaggcctc	caaggtgatc	720
cctgtcatga	tgatgggaaa	gctgggtgtcc	cggcgagct	atgaacactg	ggaatacctg	780
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agaagctctc	cagccaccac	actctctggc	ttggctctac	tggcaggcta	tattgctttc	900
gacagcttca	cctcaaattg	gcaggatgcc	ctgtttgcct	ataagatgtc	atcgggtgcag	960
atgatgtttg	gggtcaattt	attctcctgt	cttttcacag	taggtcact	actggaacag	1020
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tcctgcctcc	tctatggcca	tactgtcact	gtgggtggggg	gactgggagt	agctgtggtc	1260
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tcctgcagtt	cccctagggg	ccagtgaaga	tgggtgctgtg	ccagaagggg	caaaggcccc	1680
cagcccagtt	ggggccc					1697

&lt;210&gt; 265

&lt;211&gt; 159

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;220&gt;

&lt;400&gt; 265

gtttttcttct	ccaggctgaa	gacctgaacg	tcaagttgga	aggggagcct	tccatgcgga	60
aaccaaagca	gcggccgcgg	ccggagcccc	tcattcatccc	caccaaggcg	ggcactttca	120
tcgccccctcc	tgtctactcc	aacatcacc	cttaccaga			159

&lt;210&gt; 266

&lt;211&gt; 292

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 266

gtgggggtccc	agacttgcca	accaaagggc	cattcctgggt	atatggttct	ggcttcagct	60
ctgggtggcat	ggactatggt	atgggtgggtg	gcaaggaggc	tgggaccgag	tctcgttca	120
aacagtggac	ctcaatgatg	gaagggctgc	catctgtggc	cacacaagaa	gccaccatgc	180
acaaaaacgg	cgctatagt	gccccctggta	agacccgagg	agggtcacca	tacaaccagt	240
ttgatataat	cccaggtgac	acactgggtg	gccatacggg	tcctgctggt	ga	292

&lt;210&gt; 267

&lt;211&gt; 339

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 267

ccactgacct	tcccagaagg	tgacagccgg	cggcggatgt	tgtcaaggag	ccgagatagt	60
ccagcagtgc	ctcggtagcc	agaagacggg	ctgtctcccc	ccaaaagacg	gcgacattcg	120
atgagaagtc	accacagtga	tctcacattt	tgcgagatta	tcctgatgga	gatggagtcc	180
catgatgcag	cctggccttt	cctagagcct	gtgaaccctc	gcttggtgag	tggataccga	240
cgtgtcatca	agaaccctat	ggatttttcc	accatgcgag	aacgcctgct	ccgtggaggg	300
tacactagct	cagaagagtt	tgcagctgat	gctctgctg			339

&lt;210&gt; 268

&lt;211&gt; 153

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 268

ctgaagttct	ctcatccttg	tctggaagac	cataatagtt	actgcattaa	tggagcatgt	60
gcattccacc	atgagctgaa	gcaagccatt	tgcagatgct	ttactgggta	tacgggacaa	120
cgatgtgagc	atttgacctt	aacttcgtat	gct			153

&lt;210&gt; 269

&lt;211&gt; 153

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 269

ttgaagttct	cacacctttg	cctggaagat	cataacagtt	actgcatcaa	cggtgcttgt	60
gcattccacc	atgagctaga	gaaagccatc	tgcaggtggt	ttactgggta	tactggagaa	120
aggtgtgagc	acttgacttt	aacttcatat	gct			153

&lt;210&gt; 270

&lt;211&gt; 288

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 270

gcggccgcgc	tgtcctgct	gctgctggcg	ctgtacaccg	cgctgttgga	cggttccaaa	60
tgcaagtgtc	cccgaagg	acccaagatc	cgctacagcg	acgtgaagaa	gctggaaatg	120
aagccaaagt	accgcactg	cgaggagaag	atggttatca	tcaccaccaa	gagcgtgtcc	180
aggtaccgag	gtcaggagca	ctgcctgcac	cccaagctgc	agagcaccaa	gcgcttcac	240
aagtggatca	acgcctggaa	cgagaagcgc	agggctctacg	aagaatag		288

&lt;210&gt; 271

&lt;211&gt; 234

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 271

tccaagtgtg	agtgttcccc	gaaggggccc	aagatccgct	acagcgacgt	gaagaagctg	60
gaaatgaagc	caaagtaccc	acactgcgag	gagaagatgg	ttatcgtcac	caccaagagc	120
atgtccaggt	accggggcca	ggagcactgc	ctgcacccta	agctgcagag	caccaaaccg	180
ttcatcaagt	ggtacaatgc	ctggaacgag	aagcgcaggg	tctacgaaga	atag	234

&lt;210&gt; 272

&lt;211&gt; 234

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 272

tccaaatgca	agtgttcccc	gaagggaccc	aagatccgct	acagcgacgt	gaagaagctg	60
gaaatgaagc	caaagtaccc	gcactgcgag	gagaagatgg	ttatcatcac	caccaagagc	120
gtgtccaggt	accgaggtca	ggagcactgc	ctgcacccca	agctgcagag	caccaagcgc	180



ttcatcaagt ggtacaacgc ctggaacgag aagcgcaggg tctacgaaga atag

234

<210> 273  
 <211> 645  
 <212> DNA  
 <213> Mouse

<400> 273  
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 acctccgaca tcttggaat cagcactatg gctaactgtct ctggtgggga tgtaacctat 180  
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 tccgaggatg tgactaaagt caacctgcag gtctctcatcg tcgtcaatcg cacagcctca 420  
 aagtcacccg tgaaaatgga acaagtacaa cctcagcct caaccctat tctgagagt 480  
 tctgagacca gccagaccat aaacacgact ccaactgtga acacagccaa gactacagcc 540  
 aaggacacag ccaacaccac agccgtgacc acagccaata ccacagccaa taccacagcc 600  
 gtgaccacag ccaagaccac agccaaaagc ctggccatcc gcact 645

<210> 274  
 <211> 63  
 <212> DNA  
 <213> Mouse

<400> 274  
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 aac 63

<210> 275  
 <211> 388  
 <212> PRT  
 <213> Mouse

<400> 275  
 Met Gly Leu Glu Pro Ser Trp Tyr Leu Leu Leu Cys Leu Ala Val Ser  
 1 5 10 15  
 Gly Ala Ala Gly Thr Asp Pro Pro Thr Ala Pro Thr Thr Ala Glu Arg  
 20 25 30  
 Gln Arg Gln Pro Thr Asp Ile Ile Leu Asp Cys Phe Leu Val Thr Glu  
 35 40 45  
 Asp Arg His Arg Gly Ala Phe Ala Ser Ser Gly Asp Arg Glu Arg Ala  
 50 55 60  
 Leu Leu Val Leu Lys Gln Val Pro Val Leu Asp Asp Gly Ser Leu Glu  
 65 70 75 80  
 Gly Ile Thr Asp Phe Gln Gly Ser Thr Glu Thr Lys Gln Asp Ser Pro  
 85 90 95  
 Val Ile Phe Glu Ala Ser Val Asp Leu Val Gln Ile Pro Gln Ala Glu  
 100 105 110  
 Ala Leu Leu His Ala Asp Cys Ser Gly Lys Ala Val Thr Cys Glu Ile  
 115 120 125  
 Ser Lys Tyr Phe Leu Gln Ala Arg Gln Glu Ala Thr Phe Glu Lys Ala  
 130 135 140  
 His Trp Phe Ile Ser Asn Met Gln Val Ser Arg Gly Gly Pro Ser Val  
 145 150 155 160  
 Ser Met Val Met Lys Thr Leu Arg Asp Ala Glu Val Gly Ala Val Arg  
 165 170 175  
 His Pro Thr Leu Asn Leu Pro Leu Ser Ala Gln Gly Thr Val Lys Thr  
 180 185 190  
 Gln Val Glu Phe Gln Val Thr Ser Glu Thr Gln Thr Leu Asn His Leu  
 195 200 205  
 Leu Gly Ser Ser Val Ser Leu His Cys Ser Phe Ser Met Ala Pro Asp

210	215	220
Leu Asp Leu Thr Gly Val	Glu Trp Arg Leu Gln His	Lys Gly Ser Gly
225	230	235
Gln Leu Val Tyr Ser Trp	Lys Thr Gly Gln Gly Gln	Ala Lys Arg Lys
	245	250
Gly Ala Thr Leu Glu Pro	Glu Glu Leu Leu Arg	Ala Gly Asn Ala Ser
	260	265
Leu Thr Leu Pro Asn Leu	Thr Leu Lys Asp Glu Gly	Thr Tyr Ile Cys
	275	280
Gln Ile Ser Thr Ser Leu	Tyr Gln Ala Gln Gln	Ile Met Pro Leu Asn
	290	295
Ile Leu Ala Pro Pro Lys	Val Gln Leu His Leu	Ala Asn Lys Asp Pro
305	310	315
Leu Pro Ser Leu Val Cys	Ser Ile Ala Gly Tyr Tyr	Pro Leu Asp Val
	325	330
Gly Val Thr Trp Ile Arg	Glu Glu Leu Gly Gly	Ile Pro Ala Gln Val
	340	345
Ser Gly Ala Ser Phe Ser	Ser Leu Arg Gln Ser	Thr Met Gly Thr Tyr
	355	360
Ser Ile Ser Ser Thr Val	Met Ala Asp Pro Gly	Pro Thr Gly Ala Thr
	370	375
Tyr Thr Cys Gln		380
385		

&lt;210&gt; 276

&lt;211&gt; 151

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 276

Met Ala Glu Pro Trp Ala	Gly Gln Phe Leu Gln	Ala Leu Pro Ala Thr
1	5	10
Val Leu Gly Ala Leu Gly	Thr Leu Gly Ser Glu	Phe Leu Arg Glu Trp
	20	25
Glu Thr Gln Asp Met Arg	Val Thr Leu Phe Lys	Leu Leu Leu Leu Trp
	35	40
Leu Val Leu Ser Leu Leu	Gly Ile Gln Leu Ala	Trp Gly Phe Tyr Gly
	50	55
Asn Thr Val Thr Gly Leu	Tyr His Arg Pro Gly	Lys Trp Gln Gln Met
65	70	75
Lys Leu Ser Lys Leu Thr	Glu Asn Lys Gly Arg	Gln Gln Glu Lys Gly
	85	90
Leu Gln Arg Tyr Arg Trp	Val Cys Trp Leu Leu	Cys Cys Thr Leu Leu
	100	105
Leu Ser Arg Pro Leu Arg	Gln Leu Gln Arg Ala	Trp Val Gly Gly Leu
	115	120
Glu Tyr His Asp Ala Pro	Arg Val Ser Leu His	Cys Pro Gln Pro Cys
	130	135
Leu Gln Gln Arg Gln Val	Leu	
145	150	

&lt;210&gt; 277

&lt;211&gt; 163

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 277

Met Pro Leu Val Thr Thr	Leu Phe Tyr Ala Cys	Phe Tyr His Tyr Thr
1	5	10
Glu Ser Glu Gly Thr Phe	Ser Ser Pro Val	Asn Leu Lys Lys Thr Phe
	20	25
		30

Lys Ile Pro Asp Arg Gln Tyr Val Leu Thr Ala Leu Ala Ala Arg Ala  
 35 40 45  
 Lys Leu Arg Ala Trp Asn Asp Val Asp Ala Leu Phe Thr Thr Lys Asn  
 50 55 60  
 Trp Leu Gly Tyr Thr Lys Lys Arg Ala Pro Ile Gly Phe His Arg Val  
 65 70 75 80  
 Val Glu Ile Leu His Lys Asn Ser Ala Pro Val Gln Ile Leu Gln Glu  
 85 90 95  
 Tyr Val Asn Leu Val Glu Asp Val Asp Thr Lys Leu Asn Leu Ala Thr  
 100 105 110  
 Lys Phe Lys Cys His Asp Val Val Ile Asp Thr Cys Arg Asp Leu Lys  
 115 120 125  
 Asp Arg Gln Gln Leu Leu Ala Tyr Arg Ser Lys Val Asp Lys Gly Ser  
 130 135 140  
 Ala Glu Glu Glu Lys Ile Asp Val Ile Leu Ser Ser Ser Gln Ile Arg  
 145 150 155 160  
 Trp Lys Asn

&lt;210&gt; 278

&lt;211&gt; 330

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 278

Met Ala Gly Trp Ala Gly Ala Glu Leu Ser Val Leu Asn Pro Leu Arg  
 1 5 10 15  
 Ala Leu Trp Leu Leu Leu Ala Ala Ala Phe Leu Leu Ala Leu Leu Leu  
 20 25 30  
 Gln Leu Ala Pro Ala Arg Leu Leu Pro Ser Cys Ala Leu Phe Gln Asp  
 35 40 45  
 Leu Ile Arg Tyr Gly Lys Thr Lys Gln Ser Gly Ser Arg Arg Pro Ala  
 50 55 60  
 Val Cys Arg Ala Phe Asp Val Pro Lys Arg Tyr Phe Ser His Phe Tyr  
 65 70 75 80  
 Val Val Ser Val Leu Trp Asn Gly Ser Leu Leu Trp Phe Leu Ser Gln  
 85 90 95  
 Ser Leu Phe Leu Gly Ala Pro Phe Pro Ser Trp Leu Trp Ala Leu Leu  
 100 105 110  
 Arg Thr Leu Gly Val Thr Gln Phe Gln Ala Leu Gly Met Glu Ser Lys  
 115 120 125  
 Ala Ser Arg Ile Gln Ala Gly Glu Leu Ala Leu Ser Thr Phe Leu Val  
 130 135 140  
 Leu Val Phe Leu Trp Val His Ser Leu Arg Arg Leu Phe Glu Cys Phe  
 145 150 155 160  
 Tyr Val Ser Val Phe Ser Asn Thr Ala Ile His Val Val Gln Tyr Cys  
 165 170 175  
 Phe Gly Leu Val Tyr Tyr Val Leu Val Gly Leu Thr Val Leu Ser Gln  
 180 185 190  
 Val Pro Met Asn Asp Lys Asn Val Tyr Ala Leu Gly Lys Asn Leu Leu  
 195 200 205  
 Leu Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Met Phe Phe Trp  
 210 215 220  
 Ser Ser Ala His Gln Tyr Lys Cys His Val Ile Leu Ser Asn Leu Arg  
 225 230 235 240  
 Arg Asn Lys Lys Gly Val Val Ile His Cys Gln His Arg Ile Pro Phe  
 245 250 255  
 Gly Asp Trp Phe Glu Tyr Val Ser Ser Ala Asn Tyr Leu Ala Glu Leu  
 260 265 270  
 Met Ile Tyr Ile Ser Met Ala Val Thr Phe Gly Leu His Asn Val Thr  
 275 280 285

Trp Trp Leu Val Val Thr Tyr Val Phe Phe Ser Gln Ala Leu Ser Ala  
 290 295 300  
 Phe Phe Asn His Arg Phe Tyr Lys Ser Thr Phe Val Ser Tyr Pro Lys  
 305 310 315 320  
 His Arg Lys Ala Phe Leu Pro Phe Leu Phe  
 325 330

&lt;210&gt; 279

&lt;211&gt; 61

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 279

Met Glu Asn Ile Tyr Tyr Thr Asn Leu Ile Thr Ile Leu Gly Asn Lys  
 1 5 10 15  
 His Ala Asn Gln Met Glu Leu Asn Leu Gln Ala Leu Ile Leu Ser Pro  
 20 25 30  
 Trp Phe Ala Val Cys Ala Pro Pro Gly Phe Ala Arg Asp Gln Ala Val  
 35 40 45  
 Arg Gly Leu Ala Leu Ala Gly Arg Arg Ile Thr Val Val  
 50 55 60

&lt;210&gt; 280

&lt;211&gt; 105

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 280

Met Leu Arg Arg Gln Leu Val Trp Trp His Leu Leu Ala Leu Leu Phe  
 1 5 10 15  
 Leu Pro Phe Cys Leu Cys Gln Asp Glu Tyr Met Glu Ser Pro Gln Ala  
 20 25 30  
 Gly Gly Leu Pro Pro Asp Cys Ser Lys Cys Cys His Gly Asp Tyr Gly  
 35 40 45  
 Phe Arg Gly Tyr Gln Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Ile  
 50 55 60  
 Pro Gly Asn His Gly Asn Asn Gly Asn Asn Gly Ala Thr Gly His Glu  
 65 70 75 80  
 Gly Ala Lys Gly Gly Lys Gly Asp Lys Gly Asp Leu Gly Pro Arg Gly  
 85 90 95  
 Glu Arg Gly Gln His Gly Pro Lys Gly  
 100 105

&lt;210&gt; 281

&lt;211&gt; 27

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 281

Met Leu Lys Ala Ser Leu His Ile Leu Phe Leu Gly Ile Leu Asn Val  
 1 5 10 15  
 Pro Ile Val Asp Thr Ser Thr Lys Thr Gly Val  
 20 25

&lt;210&gt; 282

&lt;211&gt; 169

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 282

Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly

```

1           5           10           15
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg
20           25           30
Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly
35           40           45
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln
50           55           60
Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu
65           70           75           80
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr
85           90           95
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly
100          105          110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
115          120          125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
130          135          140
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145          150          155          160
Gly Glu Met Pro Pro Glu Asp Gly Met
165

```

<210> 283  
 <211> 61  
 <212> PRT  
 <213> Mouse

```

<400> 283
Met Glu Lys Gln Met Asp Ala Ser Val Ser Val Ile Phe Gly Ser Ile
1           5           10           15
Val Ile Ser Ala Phe Leu Tyr Leu Ser Leu Ala Gly Pro Trp Ala Val
20           25           30
Thr Val Thr Gln Met Arg Thr Ile Ile Thr Met Asp Gln Leu Arg
35           40           45
Asp Ala Leu Ile Leu Asp Gln Leu Lys Val Ala Val Ser
50           55           60

```

<210> 284  
 <211> 131  
 <212> PRT  
 <213> Mouse

```

<400> 284
Met Ala Pro Ser Leu Trp Lys Gly Leu Val Gly Val Gly Leu Phe Ala
1           5           10           15
Leu Ala His Ala Ala Phe Ser Ala Ala Gln His Arg Ser Tyr Met Arg
20           25           30
Leu Thr Glu Lys Glu Asp Glu Ser Leu Pro Ile Asp Ile Val Leu Gln
35           40           45
Thr Leu Leu Ala Phe Ala Val Thr Cys Tyr Gly Ile Val His Ile Ala
50           55           60
Gly Glu Phe Lys Asp Met Asp Ala Thr Ser Glu Leu Lys Asn Lys Thr
65           70           75           80
Phe Asp Thr Leu Arg Asn His Pro Ser Phe Tyr Val Phe Asn His Arg
85           90           95
Gly Arg Val Leu Phe Arg Pro Ser Asp Ala Thr Asn Ser Ser Asn Leu
100          105          110
Asp Ala Leu Ser Ser Asn Thr Ser Leu Lys Leu Arg Lys Phe Asp Ser
115          120          125
Leu Arg Arg
130

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<210> 285  
 <211> 78  
 <212> PRT  
 <213> Mouse

<400> 285  
 Gly Thr Arg Lys Pro Leu Pro Met Glu Ala His Ser Arg Arg Glu Lys  
 1 5 10 15  
 Ala Ser Gly Leu Arg Leu Ala Trp His Tyr Glu Cys Ser Gly Val Ser  
 20 25 30  
 Val Trp Trp Met Cys Val Leu Gly Trp Leu Ser Phe Leu Val Phe Leu  
 35 40 45  
 Leu Phe Ser Leu Val Cys Ser Phe Pro Ser Pro Ile Asn His Ser His  
 50 55 60  
 Met Leu Pro Cys Leu Phe Leu Arg Gly Gly Gly Ser Asn Val  
 65 70 75

<210> 286  
 <211> 206  
 <212> PRT  
 <213> Mouse

<400> 286  
 Met Leu Pro Pro Ala Ile His Leu Ser Leu Ile Pro Leu Leu Cys Ile  
 1 5 10 15  
 Leu Met Arg Asn Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu  
 20 25 30  
 Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser  
 35 40 45  
 Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Ser Thr Gly  
 50 55 60  
 Leu Asp Arg Asn Ser Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser  
 65 70 75 80  
 Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys  
 85 90 95  
 Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn  
 100 105 110  
 Trp Ile Gly Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser  
 115 120 125  
 Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln  
 130 135 140  
 Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val  
 145 150 155 160  
 Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Ser  
 165 170 175  
 His Asn Phe Glu Ser Val Ser Pro Ala Lys Pro Ala Gln His His Arg  
 180 185 190  
 Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Leu Ser  
 195 200 205

<210> 287  
 <211> 169  
 <212> PRT  
 <213> Mouse

<400> 287  
 Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly  
 1 5 10 15  
 Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg  
 20 25 30

Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly  
 35 40 45  
 Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln  
 50 55 60  
 Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu  
 65 70 75 80  
 Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr  
 85 90 95  
 Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly  
 100 105 110  
 Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe  
 115 120 125  
 Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu  
 130 135 140  
 Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu  
 145 150 155 160  
 Gly Glu Met Pro Pro Glu Asp Gly Met  
 165

<210> 288  
 <211> 114  
 <212> PRT  
 <213> Mouse

<400> 288  
 Met Ser Val Thr Ile Gly Arg Leu Ala Leu Phe Leu Ile Gly Ile Leu  
 1 5 10 15  
 Leu Cys Pro Val Ala Pro Ser Leu Thr Arg Ser Trp Pro Gly Pro Asp  
 20 25 30  
 Thr Cys Ser Leu Phe Leu Gln His Ser Leu Ser Leu Ser Leu Arg Leu  
 35 40 45  
 Gly Gln Ser Leu Glu Gly Gly Leu Ser Val Cys Phe His Val Cys Ile  
 50 55 60  
 His Ala Cys Glu Cys Val Ala Cys Cys Arg Val Leu Trp Asp Pro Lys  
 65 70 75 80  
 Pro Arg Gly Ser Ser Leu Cys Arg Trp Val Leu Gly Ser Ile Thr Cys  
 85 90 95  
 Leu Phe Met Tyr Glu Val Gly Gly Trp Thr Gln Gly Gly Leu Ile Val  
 100 105 110  
 Ser Leu

<210> 289  
 <211> 46  
 <212> PRT  
 <213> Mouse

<400> 289  
 Met His Tyr Pro Cys Leu Ala Cys Leu Phe Val Asn Val His Trp Cys  
 1 5 10 15  
 Phe Ala Trp Met Cys Ile Leu Val Lys Met Ser Glu Leu Leu Glu Leu  
 20 25 30  
 Glu Leu Glu Thr Met Val Ser Cys Leu Val Asp Val Gly Asn  
 35 40 45

<210> 290  
 <211> 199  
 <212> PRT  
 <213> Mouse

<400> 290

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Met Val Leu Pro Thr Val Leu Ile Leu Leu Leu Ser Trp Ala Ala Gly
 1          5          10          15
Leu Gly Gly Glu Thr Arg Pro Arg Ala Ala Thr Glu Arg Arg Ser Val
          20          25          30
Gly Pro Ser Ala Arg Arg Gly Ala Gly Pro Arg Val Ser Gly Leu Leu
          35          40          45
Gly Phe Cys Gln Leu Ser Gln Leu Ala Ser Ala Asp Pro Glu Arg Arg
          50          55          60
Ser Pro Arg Ala Ile Val Pro Arg Ala Pro Arg Pro Arg Ser Arg Arg
65          70          75          80
Arg Pro Cys Leu Pro Gly Phe Ser Arg Arg Phe Pro Arg Glu Arg Arg
          85          90          95
Ser Pro Gly Gln Pro Pro Ser Arg Thr Pro Gln Pro Pro Gln Pro Cys
          100          105          110
Arg Gly Pro Ser Pro Gly Thr Ala Gln Thr Arg Ser Asn Leu Arg Gly
          115          120          125
Trp Gln Arg Gly Gly Ser Ile Val Leu Gln Ala Ser Glu Arg Thr Arg
          130          135          140
Ala Gly Cys Arg Thr Pro Val Cys Val Ser His Pro Ser Ala Phe Pro
145          150          155          160
Pro Pro Arg Ala Leu Phe Gly Val Phe Val Ala Ser Ala Pro Glu Val
          165          170          175
Val Cys Val Cys Val Ser Val Val Leu Ser Val Cys Leu Leu Ser Pro
          180          185          190
Arg Gly Lys Thr Leu Val Asp
          195

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&lt;210&gt; 291

&lt;211&gt; 568

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 291

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Met Glu Leu Leu Tyr Trp Cys Leu Leu Cys Leu Leu Leu Pro Leu Thr
 1          5          10          15
Ser Arg Thr Gln Lys Leu Pro Thr Arg Asp Glu Glu Leu Phe Gln Met
          20          25          30
Gln Ile Arg Asp Lys Ala Leu Phe His Asp Ser Ser Val Ile Pro Asp
          35          40          45
Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr Pro Arg Arg Tyr
          50          55          60
Phe Phe Met Val Glu Glu Asp Asn Thr Pro Leu Ser Val Thr Val Thr
65          70          75          80
Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu Ser Leu Gln Glu Leu Pro
          85          90          95
Glu Glu Ser Ser Ala Asp Gly Ser Gly Asp Pro Glu Pro Leu Asp Gln
          100          105          110
Gln Lys Gln Gln Met Thr Asp Val Glu Gly Thr Glu Leu Phe Ser Tyr
          115          120          125
Lys Gly Asn Asp Val Glu Tyr Phe Leu Ser Ser Ser Ser Pro Ser Gly
          130          135          140
Leu Tyr Gln Leu Glu Leu Ser Thr Glu Lys Asp Thr His Phe Lys
145          150          155          160
Val Tyr Ala Thr Thr Thr Pro Glu Ser Asp Gln Pro Tyr Pro Asp Leu
          165          170          175
Pro Tyr Asp Pro Arg Val Asp Val Thr Ser Ile Gly Arg Thr Thr Val
          180          185          190
Thr Leu Ala Trp Lys Gln Ser Pro Thr Ala Ser Met Leu Lys Gln Pro
          195          200          205
Ile Glu Tyr Cys Val Val Ile Asn Lys Glu His Asn Phe Lys Ser Leu
210          215          220

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Cys Ala Ala Glu Thr Lys Met Ser Ala Asp Asp Ala Phe Met Val Ala  
 225 230 235 240  
 Pro Lys Pro Gly Leu Asp Phe Ser Pro Phe Asp Phe Ala His Phe Gly  
 245 250 255  
 Phe Pro Thr Asp Asn Leu Gly Lys Asp Arg Ser Phe Leu Ala Lys Pro  
 260 265 270  
 Ser Pro Lys Val Gly Arg His Val Tyr Trp Arg Pro Lys Val Asp Ile  
 275 280 285  
 Lys Lys Ile Cys Ile Gly Ser Lys Asn Ile Phe Thr Val Ser Asp Leu  
 290 295 300  
 Lys Pro Asn Thr Gln Tyr Tyr Phe Asp Val Phe Met Val Asn Thr Asn  
 305 310 315 320  
 Thr Asn Met Asn Thr Ala Phe Val Gly Ala Phe Ala Arg Thr Lys Glu  
 325 330 335  
 Glu Ala Lys Gln Lys Thr Val Glu Leu Lys Asp Gly Arg Val Thr Asp  
 340 345 350  
 Val Val Val Lys Arg Lys Gly Lys Lys Phe Leu Arg Phe Ala Pro Val  
 355 360 365  
 Ser Ser His Gln Lys Val Thr Leu Phe Ile His Ser Cys Met Asp Thr  
 370 375 380  
 Val Gln Val Gln Val Arg Arg Asp Gly Lys Leu Leu Ser Gln Asn  
 385 390 395 400  
 Val Glu Gly Ile Arg Gln Phe Gln Leu Arg Gly Lys Pro Lys Gly Lys  
 405 410 415  
 Tyr Leu Ile Arg Leu Lys Gly Asn Lys Lys Gly Ala Ser Met Leu Lys  
 420 425 430  
 Ile Leu Ala Thr Thr Arg Pro Ser Lys His Ala Phe Pro Ser Leu Pro  
 435 440 445  
 Asp Asp Thr Arg Ile Lys Ala Phe Asp Lys Leu Arg Thr Cys Ser Ser  
 450 455 460  
 Val Thr Val Ala Trp Leu Gly Thr Gln Glu Arg Lys Phe Cys Ile  
 465 470 475 480  
 Tyr Arg Lys Glu Val Gly Gly Asn Tyr Ser Glu Glu Gln Lys Arg Arg  
 485 490 495  
 Glu Arg Asn Gln Cys Leu Gly Pro Asp Thr Arg Lys Lys Ser Glu Lys  
 500 505 510  
 Val Leu Cys Lys Tyr Phe His Ser Gln Asn Leu Gln Lys Ala Val Thr  
 515 520 525  
 Thr Glu Thr Ile Arg Asp Leu Gln Pro Gly Lys Ser Tyr Leu Leu Asp  
 530 535 540  
 Val Tyr Val Val Gly His Gly Gly His Ser Val Lys Tyr Gln Ser Lys  
 545 550 555 560  
 Leu Val Lys Thr Arg Lys Val Cys  
 565

<210> 292  
 <211> 123  
 <212> PRT  
 <213> Mouse

<400> 292  
 Met Leu Thr Glu Pro Ala Gln Leu Phe Val His Lys Lys Asn Gln Pro  
 1 5 10 15  
 Pro Ser His Ser Ser Leu Arg Leu His Phe Arg Thr Leu Ala Gly Ala  
 20 25 30  
 Leu Ala Leu Ser Ser Thr Gln Met Ser Trp Gly Leu Gln Ile Leu Pro  
 35 40 45  
 Cys Leu Ser Leu Ile Leu Leu Leu Trp Asn Gln Val Pro Gly Leu Glu  
 50 55 60  
 Gly Gln Glu Phe Arg Phe Gly Ser Cys Gln Val Thr Gly Val Val Leu  
 65 70 75 80

Pro Glu Leu Trp Glu Ala Phe Trp Thr Val Lys Asn Thr Val Gln Thr  
                   85                  90                  95  
 Gln Asp Asp Ile Thr Ser Ile Arg Leu Leu Lys Pro Gln Val Leu Arg  
                   100                  105                  110  
 Asn Val Ser Val Ile Arg Trp Glu Gly Asp Ser  
                   115                  120

<210> 293  
 <211> 66  
 <212> PRT  
 <213> Mouse

<400> 293  
 Met Asp Val Trp Ser Gly Leu Pro Leu Glu Thr Leu Trp Ile Tyr Glu  
   1                  5                  10                  15  
 Ala Val Leu Pro Trp Leu Leu Met Gly Gln Gly His Ala Trp Val Cys  
                   20                  25                  30  
 Gly Pro Ile Ala Leu Trp Val Phe Val Asn Val Pro Gly Leu Cys Tyr  
                   35                  40                  45  
 His Gln Lys Pro Phe Arg Cys Pro Trp Ser Gly Leu Leu Pro Glu Ala  
                   50                  55                  60  
 Leu Cys  
 65

<210> 294  
 <211> 294  
 <212> PRT  
 <213> Rat

<400> 294  
 Met Thr Val Phe Arg Lys Val Thr Thr Met Ile Ser Trp Met Leu Leu  
   1                  5                  10                  15  
 Ala Cys Ala Leu Pro Cys Ala Ala Asp Pro Met Leu Gly Ala Phe Ala  
                   20                  25                  30  
 Arg Arg Asp Phe Gln Lys Gly Gly Pro Gln Leu Val Cys Ser Leu Pro  
                   35                  40                  45  
 Gly Pro Gln Gly Pro Pro Gly Pro Pro Gly Ala Pro Gly Ser Ser Gly  
                   50                  55                  60  
 Met Val Gly Arg Met Gly Phe Pro Gly Lys Asp Gly Gln Asp Gly Gln  
   65                  70                  75                  80  
 Asp Gly Asp Arg Gly Asp Ser Gly Glu Glu Gly Pro Pro Gly Arg Thr  
                   85                  90                  95  
 Gly Asn Arg Gly Lys Gln Gly Pro Lys Gly Lys Ala Gly Ala Ile Gly  
                   100                  105                  110  
 Arg Ala Gly Pro Arg Gly Pro Lys Gly Val Ser Gly Thr Pro Gly Lys  
                   115                  120                  125  
 His Gly Ile Pro Gly Lys Lys Gly Pro Lys Gly Lys Lys Gly Glu Pro  
                   130                  135                  140  
 Gly Leu Pro Gly Pro Cys Ser Cys Gly Ser Ser Arg Ala Lys Ser Ala  
   145                  150                  155                  160  
 Phe Ser Val Ala Val Thr Lys Ser Tyr Pro Arg Glu Arg Leu Pro Ile  
                   165                  170                  175  
 Lys Phe Asp Lys Ile Leu Met Asn Glu Gly Gly His Tyr Asn Ala Ser  
                   180                  185                  190  
 Ser Gly Lys Phe Val Cys Ser Val Pro Gly Ile Tyr Tyr Phe Thr Tyr  
                   195                  200                  205  
 Asp Ile Thr Leu Ala Asn Lys His Leu Ala Ile Gly Leu Val His Asn  
                   210                  215                  220  
 Gly Gln Tyr Arg Ile Arg Thr Phe Asp Ala Asn Thr Gly Asn His Asp  
   225                  230                  235                  240  
 Val Ala Ser Gly Ser Thr Ile Leu Ala Leu Lys Glu Gly Asp Glu Val

<210>	295
<211>	243
<212>	PRT
<213>	Rat

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<210> 296
<211> 444
<212> PRT
<213> Rat
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112

Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val  
 65 70 75 80  
 Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile  
 85 90 95  
 Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr  
 100 105 110  
 Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn  
 115 120 125  
 Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg  
 130 135 140  
 Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu  
 145 150 155 160  
 Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser  
 165 170 175  
 Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe  
 180 185 190  
 Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp  
 195 200 205  
 Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser  
 210 215 220  
 Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys  
 225 230 235 240  
 Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu  
 245 250 255  
 Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu  
 260 265 270  
 Gln His Asp Val Leu Lys Leu Glu Phe Glu Arg His Asp Pro Val Asp  
 275 280 285  
 Gly Arg Ile Ser Glu Arg Gln Phe Gly Gly Met Leu Leu Ala Tyr Ser  
 290 295 300  
 Gly Val Gln Ser Lys Lys Leu Thr Ala Met Gln Arg Gln Leu Lys Lys  
 305 310 315 320  
 His Phe Lys Asp Gly Lys Gly Leu Thr Phe Gln Glu Val Glu Asn Phe  
 325 330 335  
 Phe Thr Phe Leu Lys Asn Ile Asn Asp Val Asp Thr Ala Leu Ser Phe  
 340 345 350  
 Tyr His Met Ala Gly Ala Ser Leu Asp Lys Val Thr Met Gln Gln Val  
 355 360 365  
 Ala Arg Thr Val Ala Lys Val Glu Leu Ser Asp His Val Cys Asp Val  
 370 375 380  
 Val Phe Ala Leu Phe Asp Cys Asp Gly Asn Gly Glu Leu Ser Asn Lys  
 385 390 395 400  
 Glu Phe Val Ser Ile Met Lys Gln Arg Leu Met Arg Gly Leu Glu Lys  
 405 410 415  
 Pro Lys Asp Met Gly Phe Thr Arg Leu Met Gln Ala Met Trp Lys Cys  
 420 425 430  
 Ala Gln Glu Thr Ala Trp Asp Phe Ala Leu Pro Lys  
 435 440

&lt;210&gt; 297

&lt;211&gt; 65

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 297

Met Thr Met Leu His Leu Ala Val Ile Phe Leu Phe Ser Ala Leu Ser  
 1 5 10 15  
 Arg Ala Leu Val Gln Cys Ser Ser His Arg Ala Arg Val Val Leu Ser  
 20 25 30  
 Trp Ala Asp Tyr Leu Arg Arg Val Ala Pro Thr Ala Leu Ala Thr Ala  
 35 40 45

Leu Asp Val Gly Leu Ser Asn Trp Ser Phe Leu Tyr Val Thr Val Ser  
 50 55 60

Leu  
 65

<210> 298  
 <211> 52  
 <212> PRT  
 <213> Human

<400> 298  
 Met Lys Ile Asn Ile Ile Gln Gly Ser Ile Met Ile Leu Leu Ile Cys  
 1 5 10 15  
 Leu Ser Gln Thr Cys Thr Ser Leu Pro Val Gln Glu Ala Leu Ile Thr  
 20 25 30  
 Phe Cys His Leu Tyr Phe Thr Tyr Cys Tyr Ser Gly Asn Ser Asn Lys  
 35 40 45  
 Met Gln Val Leu  
 50

<210> 299  
 <211> 41  
 <212> PRT  
 <213> Human

<400> 299  
 Met Pro Cys Val Leu Phe Phe Phe Phe Phe Leu Ser Thr Ser Lys Ser  
 1 5 10 15  
 Met Ile Tyr Ser Ser Leu Met Leu Gly Leu Tyr Ile Pro Ser Glu Ala  
 20 25 30  
 Cys Val Leu Gly Leu Lys Phe Lys Phe  
 35 40

<210> 300  
 <211> 80  
 <212> PRT  
 <213> Mouse

<400> 300  
 Met Val Trp Gly Thr Leu Leu Gly Arg Val Leu Ala Ala Leu Leu Asn  
 1 5 10 15  
 Ile Val Pro Thr Glu Ser Ser Tyr Arg Ser Pro Ser Phe Leu Ala Gly  
 20 25 30  
 Phe Arg Phe Cys Cys Ser Pro Trp Ser Gln His Phe Gly Cys Gly Arg  
 35 40 45  
 Leu Thr Ser Cys Leu Pro Pro Cys Val Asp Arg Val Val Lys Thr Tyr  
 50 55 60  
 Ser Ser Pro Pro Cys Leu Ser Val Asn Gly His Asp Val Thr Ile Cys  
 65 70 75 80

<210> 301  
 <211> 82  
 <212> PRT  
 <213> Mouse

<400> 301  
 Met Gly Ser Val Leu Thr Ser Cys Phe Cys Val Gly Gly Ser Ala Glu  
 1 5 10 15  
 Ala Trp Asn Trp Leu Pro Ser Ala Ser Ser Leu Phe Pro Cys Cys Ile  
 20 25 30  
 Ala Thr Leu Leu Pro Leu Leu Phe Leu Leu Pro His Leu His Ser Thr

35 40 45  
 Leu Ser Arg Val Gln Arg Leu Asn Phe Asn Ile Gly His Leu Gly Val  
 50 55 60  
 Tyr Leu Tyr Val Asn Asn Asp Ile Arg Ser Arg Val Thr Pro Leu Leu  
 65 70 75 80  
 Ser Ser

&lt;210&gt; 302

&lt;211&gt; 411

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 302

Met Pro Thr Met Trp Pro Leu Leu His Val Leu Trp Leu Ala Leu Val  
 1 5 10 15  
 Cys Gly Ser Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala  
 20 25 30  
 Ala Ser Lys Thr Leu Leu Glu Lys Thr Gln Phe Ser Asp Lys Pro Val  
 35 40 45  
 Gln Asp Arg Gly Leu Val Val Thr Asp Ile Lys Ala Glu Asp Val Val  
 50 55 60  
 Leu Glu His Arg Ser Tyr Cys Ser Ala Arg Ala Arg Glu Arg Asn Phe  
 65 70 75 80  
 Ala Gly Glu Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr  
 85 90 95  
 Asp Val Ala Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val  
 100 105 110  
 Trp Leu Gln Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Ile Thr Gly  
 115 120 125  
 Leu His Asp Val Asp Gln Gly Trp Met Arg Ala Val Lys Lys His Ala  
 130 135 140  
 Lys Gly Val Arg Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr  
 145 150 155 160  
 Asp Asp Phe Arg Ser Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu  
 165 170 175  
 Ser Lys Thr Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe  
 180 185 190  
 Val Val Glu Val Trp Ser Gln Leu Leu Ser Gln Lys His Val Gly Leu  
 195 200 205  
 Ile His Met Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu  
 210 215 220  
 Leu Val Ile Leu Val Ile Pro Pro Ala Val Thr Pro Gly Thr Asp Gln  
 225 230 235 240  
 Leu Gly Met Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Ile Leu  
 245 250 255  
 Asp Gly Phe Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ser Gln Gln Pro  
 260 265 270  
 Gly Pro Asn Ala Pro Leu Ser Trp Ile Arg Ala Cys Val Gln Val Leu  
 275 280 285  
 Asp Pro Lys Ser Gln Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe  
 290 295 300  
 Tyr Gly Met Asp Tyr Ala Ala Ser Lys Asp Ala Arg Glu Pro Val Ile  
 305 310 315 320  
 Gly Ala Arg Ala Val Leu Lys Val Ala Leu Pro Leu Ala Val Ser Ser  
 325 330 335  
 Gln Gln Ile Trp Thr Leu Gly Arg Gly Gly Ser Thr Ser Ala Leu Leu  
 340 345 350  
 Leu Ala Gly Leu Gly Leu Ala Ser Glu Pro Cys Thr Lys Ser Glu Glu  
 355 360 365  
 Val Pro Lys Lys Ser Leu Leu Asp Thr Val Trp His Trp Gln Gly Glu

370 375 380  
 Pro Gly Ala Leu Cys Arg Gly Arg Leu His Thr Trp Ile Leu Val Ser  
 385 390 395 400  
 Ala Val Pro Gln Ala Cys Thr Cys Leu Phe Gln  
 405 410

<210> 303  
 <211> 617  
 <212> PRT  
 <213> Mouse

<400> 303  
 Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Leu Ser Leu Pro Leu Leu  
 1 5 10 15  
 Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala Cys Pro Cys Leu Arg  
 20 25 30  
 Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe  
 35 40 45  
 Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys  
 50 55 60  
 Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser  
 65 70 75 80  
 Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His  
 85 90 95  
 Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr  
 100 105 110  
 Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu  
 115 120 125  
 Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu  
 130 135 140  
 Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala  
 145 150 155 160  
 Ser Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser  
 165 170 175  
 Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly Gly His Thr Val Asp  
 180 185 190  
 Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys Ile Glu Ala Ser Tyr  
 195 200 205  
 Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser Trp  
 210 215 220  
 Pro Glu Ala Tyr Gly Ser Asp Phe Trp Gln Ser Ile Arg Phe Thr Asp  
 225 230 235 240  
 Tyr Ser Gln His Asn Gln Met Val Met Ala Leu Thr Leu Arg Cys Pro  
 245 250 255  
 Leu Lys Leu Glu Ala Ser Leu Cys Trp Arg Gln Asp Pro Leu Thr Pro  
 260 265 270  
 Cys Glu Thr Leu Pro Asn Ala Thr Ala Gln Glu Ser Glu Gly Trp Tyr  
 275 280 285  
 Ile Leu Glu Asn Val Asp Leu His Pro Gln Leu Cys Phe Lys Phe Ser  
 290 295 300  
 Phe Glu Asn Ser Ser His Val Glu Cys Pro His Gln Ser Gly Ser Leu  
 305 310 315 320  
 Pro Ser Trp Thr Val Ser Met Asp Thr Gln Ala Gln Gln Leu Thr Leu  
 325 330 335  
 His Phe Ser Ser Arg Thr Tyr Ala Thr Phe Ser Ala Ala Trp Ser Asp  
 340 345 350  
 Pro Gly Leu Gly Pro Asp Thr Pro Met Pro Pro Val Tyr Ser Ile Ser  
 355 360 365  
 Gln Thr Gln Gly Ser Val Pro Val Thr Leu Asp Leu Ile Ile Pro Phe  
 370 375 380  
 Leu Arg Gln Glu Asn Cys Ile Leu Val Trp Arg Ser Asp Val His Phe

385					390					395				400	
Ala	Trp	Lys	His	Val	Leu	Cys	Pro	Asp	Asp	Ala	Pro	Tyr	Pro	Thr	Gln
				405					410					415	
Leu	Leu	Leu	Arg	Ser	Leu	Gly	Ser	Gly	Arg	Thr	Arg	Pro	Val	Leu	Leu
			420					425					430		
Leu	His	Ala	Ala	Asp	Ser	Glu	Ala	Gln	Arg	Arg	Leu	Val	Gly	Ala	Leu
	435						440					445			
Ala	Glu	Leu	Leu	Arg	Thr	Ala	Leu	Gly	Gly	Gly	Arg	Asp	Val	Ile	Val
	450					455				460					
Asp	Leu	Trp	Glu	Gly	Thr	His	Val	Ala	Arg	Ile	Gly	Pro	Leu	Pro	Trp
465					470				475					480	
Leu	Trp	Ala	Ala	Arg	Glu	Arg	Val	Ala	Arg	Glu	Gln	Gly	Thr	Val	Leu
			485					490						495	
Leu	Leu	Trp	Asn	Cys	Ala	Gly	Pro	Ser	Thr	Ala	Cys	Ser	Gly	Asp	Pro
			500					505					510		
Gln	Ala	Ala	Ser	Leu	Arg	Thr	Leu	Leu	Cys	Ala	Ala	Pro	Arg	Pro	Leu
	515						520					525			
Leu	Leu	Ala	Tyr	Phe	Ser	Arg	Leu	Cys	Ala	Lys	Gly	Asp	Ile	Pro	Arg
	530					535				540					
Pro	Leu	Arg	Ala	Leu	Pro	Arg	Tyr	Arg	Leu	Leu	Arg	Asp	Leu	Pro	Arg
545					550				555					560	
Leu	Leu	Arg	Ala	Leu	Asp	Ala	Gln	Pro	Ala	Thr	Leu	Ala	Ser	Ser	Trp
			565					570						575	
Ser	His	Leu	Gly	Ala	Lys	Arg	Cys	Leu	Lys	Asn	Arg	Leu	Glu	Gln	Cys
		580					585						590		
His	Leu	Leu	Glu	Leu	Glu	Ala	Ala	Lys	Asp	Asp	Tyr	Gln	Gly	Ser	Thr
	595					600						605			
Asn	Ser	Pro	Cys	Gly	Phe	Ser	Cys	Leu							
	610					615									

&lt;210&gt; 304

&lt;211&gt; 72

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 304

Met	Ser	Ala	Ile	Phe	Asn	Phe	Gln	Ser	Leu	Leu	Thr	Val	Ile	Leu	Leu
1				5					10					15	
Leu	Ile	Cys	Thr	Cys	Ala	Tyr	Ile	Arg	Ser	Leu	Ala	Pro	Ser	Ile	Leu
		20						25					30		
Asp	Arg	Asn	Lys	Thr	Gly	Leu	Leu	Gly	Ile	Phe	Trp	Lys	Cys	Ala	Arg
		35				40						45			
Ile	Gly	Glu	Arg	Lys	Ser	Pro	Tyr	Val	Ala	Ile	Cys	Cys	Ile	Val	Met
	50				55						60				
Ala	Phe	Ser	Ile	Leu	Phe	Ile	Gln								
65					70										

&lt;210&gt; 305

&lt;211&gt; 649

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 305

Met	Ile	Ser	Pro	Ala	Trp	Ser	Leu	Phe	Leu	Ile	Gly	Thr	Lys	Ile	Gly
1				5					10					15	
Leu	Phe	Phe	Gln	Val	Ala	Pro	Leu	Ser	Val	Val	Ala	Lys	Ser	Cys	Pro
		20						25					30		
Ser	Val	Cys	Arg	Cys	Asp	Ala	Gly	Phe	Ile	Tyr	Cys	Asn	Asp	Arg	Ser
		35				40						45			
Leu	Thr	Ser	Ile	Pro	Val	Gly	Ile	Pro	Glu	Asp	Ala	Thr	Thr	Leu	Tyr
	50					55					60				



Leu	Gln	Asn	Asn	Gln	Ile	Asn	Asn	Val	Gly	Ile	Pro	Ser	Asp	Leu	Lys
65					70					75					80
Asn	Leu	Leu	Lys	Val	Gln	Arg	Ile	Tyr	Leu	Tyr	His	Asn	Ser	Leu	Asp
			85						90					95	
Glu	Phe	Pro	Thr	Asn	Leu	Pro	Lys	Tyr	Val	Lys	Glu	Leu	His	Leu	Gln
			100					105					110		
Glu	Asn	Asn	Ile	Arg	Thr	Ile	Thr	Tyr	Asp	Ser	Leu	Ser	Lys	Ile	Pro
	115						120					125			
Tyr	Leu	Glu	Glu	Leu	His	Leu	Asp	Asp	Asn	Ser	Val	Ser	Ala	Val	Ser
	130					135					140				
Ile	Glu	Glu	Gly	Ala	Phe	Arg	Asp	Ser	Asn	Tyr	Leu	Arg	Leu	Leu	Phe
145					150					155					160
Leu	Ser	Arg	Asn	His	Leu	Ser	Thr	Ile	Pro	Gly	Gly	Leu	Pro	Arg	Thr
			165						170					175	
Ile	Glu	Glu	Leu	Arg	Leu	Asp	Asp	Asn	Arg	Ile	Ser	Thr	Ile	Ser	Ser
			180					185					190		
Pro	Ser	Leu	His	Gly	Leu	Thr	Ser	Leu	Lys	Arg	Leu	Val	Leu	Asp	Gly
	195						200					205			
Asn	Leu	Leu	Asn	Asn	His	Gly	Leu	Gly	Asp	Lys	Val	Phe	Phe	Asn	Leu
	210					215					220				
Val	Asn	Leu	Thr	Glu	Leu	Ser	Leu	Val	Arg	Asn	Ser	Leu	Thr	Ala	Ala
225					230				235						240
Pro	Val	Asn	Leu	Pro	Gly	Thr	Ser	Leu	Arg	Lys	Leu	Tyr	Leu	Gln	Asp
			245						250					255	
Asn	His	Ile	Asn	Arg	Val	Pro	Pro	Asn	Ala	Phe	Ser	Tyr	Leu	Arg	Gln
			260					265						270	
Leu	Tyr	Arg	Leu	Asp	Met	Ser	Asn	Asn	Asn	Leu	Ser	Asn	Leu	Pro	Gln
	275						280					285			
Gly	Ile	Phe	Asp	Asp	Leu	Asp	Asn	Ile	Thr	Gln	Leu	Ile	Leu	Arg	Asn
	290					295					300				
Asn	Pro	Trp	Tyr	Cys	Gly	Cys	Lys	Met	Lys	Trp	Val	Arg	Asp	Trp	Leu
305					310					315					320
Gln	Ser	Leu	Pro	Val	Lys	Val	Asn	Val	Arg	Gly	Leu	Met	Cys	Gln	Ala
			325						330					335	
Pro	Glu	Lys	Val	Arg	Gly	Met	Ala	Ile	Lys	Asp	Leu	Ser	Ala	Glu	Leu
			340					345					350		
Phe	Asp	Cys	Lys	Asp	Ser	Gly	Ile	Val	Ser	Thr	Ile	Gln	Ile	Thr	Thr
	355						360					365			
Ala	Ile	Pro	Asn	Thr	Ala	Tyr	Pro	Ala	Gln	Gly	Gln	Trp	Pro	Ala	Pro
	370					375					380				
Val	Thr	Lys	Gln	Pro	Asp	Ile	Lys	Asn	Pro	Lys	Leu	Ile	Lys	Asp	Gln
385					390					395					400
Arg	Thr	Thr	Gly	Ser	Pro	Ser	Arg	Lys	Thr	Ile	Leu	Ile	Thr	Val	Lys
			405						410					415	
Ser	Val	Thr	Pro	Asp	Thr	Ile	His	Ile	Ser	Trp	Arg	Leu	Ala	Leu	Pro
			420					425					430		
Met	Thr	Ala	Leu	Arg	Leu	Ser	Trp	Leu	Lys	Leu	Gly	His	Ser	Pro	Ala
	435						440					445			
Phe	Gly	Ser	Ile	Thr	Glu	Thr	Ile	Val	Thr	Gly	Glu	Arg	Ser	Glu	Tyr
	450					455					460				
Leu	Val	Thr	Ala	Leu	Glu	Pro	Glu	Ser	Pro	Tyr	Arg	Val	Cys	Met	Val
465					470					475					480
Pro	Met	Glu	Thr	Ser	Asn	Leu	Tyr	Leu	Phe	Asp	Glu	Thr	Pro	Val	Cys
			485						490					495	
Ile	Glu	Thr	Gln	Thr	Ala	Pro	Leu	Arg	Met	Tyr	Asn	Pro	Thr	Thr	Thr
			500					505					510		
Leu	Asn	Arg	Glu	Gln	Glu	Lys	Glu	Pro	Tyr	Lys	Asn	Pro	Asn	Leu	Pro
	515						520					525			
Leu	Ala	Ala	Ile	Ile	Gly	Gly	Ala	Val	Ala	Leu	Val	Ser	Ile	Ala	Leu
	530					535					540				
Leu	Ala	Leu	Val	Cys	Trp	Tyr	Val	His	Arg	Asn	Gly	Ser	Leu	Phe	Ser

545                      550                      555                      560  
 Arg Asn Cys Ala Tyr Ser Lys Gly Arg Arg Arg Lys Asp Asp Tyr Ala  
                                  565                      570                      575  
 Glu Ala Gly Thr Lys Lys Asp Asn Ser Ile Leu Glu Ile Arg Glu Thr  
                                  580                      585                      590  
 Ser Phe Gln Met Leu Pro Ile Ser Asn Glu Pro Ile Ser Lys Glu Glu  
                                  595                      600                      605  
 Phe Val Ile His Thr Ile Phe Pro Pro Asn Gly Met Asn Leu Tyr Lys  
                                  610                      615                      620  
 Asn Asn Leu Ser Glu Ser Ser Ser Asn Arg Ser Tyr Arg Asp Ser Gly  
 625                      630                      635                      640  
 Ile Pro Asp Ser Asp His Ser His Ser  
                                  645

<210> 306  
 <211> 150  
 <212> PRT  
 <213> Rat

<400> 306  
 Met Ala Ala Pro Met Asp Arg Thr His Gly Gly Arg Ala Ala Arg Ala  
 1                      5                      10                      15  
 Leu Arg Arg Ala Leu Ala Leu Ala Ser Leu Ala Gly Leu Leu Ser  
                                  20                      25                      30  
 Gly Leu Ala Gly Ala Leu Pro Thr Leu Gly Pro Gly Trp Arg Arg Gln  
                                  35                      40                      45  
 Asn Pro Glu Pro Pro Ala Ser Arg Thr Arg Ser Leu Leu Leu Asp Ala  
                                  50                      55                      60  
 Ala Ser Gly Gln Leu Arg Leu Glu Tyr Gly Phe His Pro Asp Ala Val  
 65                      70                      75                      80  
 Ala Trp Ala Asn Leu Thr Asn Ala Ile Arg Glu Thr Gly Trp Ala Tyr  
                                  85                      90                      95  
 Leu Asp Leu Gly Thr Asn Gly Ser Tyr Lys Trp Ile Pro Arg Ala Ala  
                                  100                      105                      110  
 Gly Leu Cys Ser Trp Cys Gly Gly Leu Cys Val Arg Gly Ala His  
                                  115                      120                      125  
 Leu His Ala Leu Asp Glu His Gly Gly Gln Leu Leu Arg Pro Leu Arg  
                                  130                      135                      140  
 Val Arg Ser Arg Leu Leu  
 145                      150

<210> 307  
 <211> 580  
 <212> PRT  
 <213> Rat

<400> 307  
 Met Ala Ala Ala Met Pro Leu Gly Leu Ser Leu Leu Leu Leu Val Leu  
 1                      5                      10                      15  
 Val Gly Gln Gly Cys Cys Gly Arg Val Glu Gly Pro Arg Asp Ser Leu  
                                  20                      25                      30  
 Arg Glu Glu Leu Val Ile Thr Pro Leu Pro Ser Gly Asp Val Ala Ala  
                                  35                      40                      45  
 Thr Phe Gln Phe Arg Thr Arg Trp Asp Ser Asp Leu Gln Arg Glu Gly  
                                  50                      55                      60  
 Val Ser His Tyr Arg Leu Phe Pro Lys Ala Leu Gly Gln Leu Ile Ser  
 65                      70                      75                      80  
 Lys Tyr Ser Leu Arg Glu Leu His Leu Ser Phe Thr Gln Gly Phe Trp  
                                  85                      90                      95  
 Arg Thr Arg Tyr Trp Gly Pro Pro Phe Leu Gln Ala Pro Ser Gly Ala  
                                  100                      105                      110

Glu Leu Trp Val Trp Phe Gln Asp Thr Val Thr Asp Val Asp Lys Ser  
 115 120 125  
 Trp Lys Glu Leu Ser Asn Val Leu Ser Gly Ile Phe Cys Ala Ser Leu  
 130 135 140  
 Asn Phe Ile Asp Ser Thr Asn Thr Val Thr Pro Thr Ala Ser Phe Lys  
 145 150 155 160  
 Pro Leu Gly Leu Ala Asn Asp Thr Asp His Tyr Phe Leu Arg Tyr Ala  
 165 170 175  
 Val Leu Pro Arg Glu Val Val Cys Thr Glu Asn Leu Thr Pro Trp Lys  
 180 185 190  
 Lys Leu Leu Pro Cys Ser Ser Lys Ala Gly Leu Ser Val Leu Leu Lys  
 195 200 205  
 Ala Asp Arg Leu Phe His Thr Ser Tyr His Ser Gln Ala Val His Ile  
 210 215 220  
 Arg Pro Ile Cys Arg Asn Ala His Cys Thr Ser Ile Ser Trp Glu Leu  
 225 230 235 240  
 Arg Gln Thr Leu Ser Val Val Phe Asp Ala Phe Ile Thr Gly Gln Gly  
 245 250 255  
 Lys Lys Asp Trp Ser Leu Phe Arg Met Phe Ser Arg Thr Leu Thr Glu  
 260 265 270  
 Ala Cys Pro Leu Ala Ser Gln Ser Leu Val Tyr Val Asp Ile Thr Gly  
 275 280 285  
 Tyr Ser Gln Asp Asn Glu Thr Leu Glu Val Ser Pro Pro Pro Thr Ser  
 290 295 300  
 Thr Tyr Gln Asp Val Ile Leu Gly Thr Arg Lys Thr Tyr Ala Val Tyr  
 305 310 315 320  
 Asp Leu Phe Asp Thr Ala Met Ile Asn Asn Ser Arg Asn Leu Asn Ile  
 325 330 335  
 Gln Leu Lys Trp Lys Arg Pro Pro Asp Asn Glu Ala Leu Pro Val Pro  
 340 345 350  
 Phe Leu His Ala Gln Arg Tyr Val Ser Gly Tyr Gly Leu Gln Lys Gly  
 355 360 365  
 Glu Leu Ser Thr Leu Leu Tyr Asn Ser His Pro Tyr Arg Ala Phe Pro  
 370 375 380  
 Val Leu Leu Leu Asp Ala Val Pro Trp Tyr Leu Arg Leu Tyr Val His  
 385 390 395 400  
 Thr Leu Thr Ile Thr Ser Lys Gly Lys Asp Asn Lys Pro Ser Tyr Ile  
 405 410 415  
 His Tyr Gln Pro Ala Gln Asp Arg Gln Gln Pro His Leu Leu Glu Met  
 420 425 430  
 Leu Ile Gln Leu Pro Ala Asn Ser Val Thr Lys Val Ser Ile Gln Phe  
 435 440 445  
 Glu Arg Ala Leu Leu Lys Trp Thr Glu Tyr Thr Pro Asp Pro Asn His  
 450 455 460  
 Gly Phe Tyr Val Ser Pro Ser Val Leu Ser Ala Leu Val Pro Ser Met  
 465 470 475 480  
 Val Ala Ala Lys Pro Val Asp Trp Glu Glu Ser Pro Leu Phe Asn Thr  
 485 490 495  
 Leu Phe Pro Val Ser Asp Gly Ser Ser Tyr Phe Val Arg Leu Tyr Thr  
 500 505 510  
 Glu Pro Leu Leu Val Asn Leu Pro Thr Pro Asp Phe Ser Met Pro Tyr  
 515 520 525  
 Asn Val Ile Cys Leu Thr Cys Thr Val Val Ala Val Cys Tyr Gly Ser  
 530 535 540  
 Phe Tyr Asn Leu Leu Thr Arg Thr Phe His Ile Glu Glu Pro Lys Ser  
 545 550 555 560  
 Gly Gly Leu Ala Lys Arg Leu Ala Asn Leu Ile Arg Arg Ala Arg Gly  
 565 570 575  
 Val Pro Pro Leu  
 580

&lt;210&gt; 308

&lt;211&gt; 283

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 308

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Met Thr Ser Gly Pro Gly Gly Pro Ala Ala Ala Thr Gly Gly Gly Lys
 1          5          10          15
Asp Thr His Gln Trp Tyr Val Cys Asn Arg Glu Lys Leu Cys Glu Ser
      20          25          30
Leu Gln Ser Val Phe Val Gln Ser Tyr Leu Asp Gln Gly Thr Gln Ile
      35          40          45
Phe Leu Asn Asn Ser Ile Glu Lys Ser Gly Trp Leu Phe Ile Gln Leu
      50          55          60
Tyr His Ser Phe Val Ser Ser Val Phe Ser Leu Phe Met Ser Arg Thr
      65          70          75          80
Ser Ile Asn Gly Leu Leu Gly Arg Gly Ser Met Phe Val Phe Ser Pro
      85          90          95
Asp Gln Phe Gln Arg Leu Leu Lys Ile Asn Pro Asp Trp Lys Thr His
      100          105          110
Arg Leu Leu Asp Leu Gly Ala Gly Asp Gly Glu Val Thr Lys Ile Met
      115          120          125
Ser Pro His Phe Glu Glu Ile Tyr Ala Thr Glu Leu Ser Glu Thr Met
      130          135          140
Ile Trp Gln Leu Gln Lys Lys Tyr Arg Val Leu Gly Ile Asn Glu
      145          150          155          160
Trp Gln Asn Thr Gly Phe Gln Tyr Asp Val Ile Ser Cys Leu Asn Leu
      165          170          175
Leu Asp Arg Cys Asp Gln Pro Leu Thr Leu Leu Lys Asp Ile Arg Ser
      180          185          190
Val Leu Glu Pro Thr Gln Gly Arg Val Ile Leu Ala Leu Val Leu Pro
      195          200          205
Phe His Pro Tyr Val Glu Asn Val Gly Gly Lys Trp Glu Lys Pro Ser
      210          215          220
Glu Ile Leu Glu Ile Lys Gly Gln Asn Trp Glu Glu Gln Val Asn Ser
      225          230          235          240
Leu Pro Glu Val Phe Arg Lys Ala Gly Phe Val Ile Glu Ala Phe Thr
      245          250          255
Arg Leu Pro Tyr Leu Cys Glu Gly Asp Met Tyr Asn Asp Tyr Tyr Val
      260          265          270
Leu Asp Asp Ala Val Phe Val Leu Arg Pro Val
      275          280

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&lt;210&gt; 309

&lt;211&gt; 37

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 309

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Met Leu Trp Val Leu Leu Ser Leu Thr Pro Leu Leu Ser Pro Leu Ile
 1          5          10          15
Phe Phe Pro Val Lys Thr Val Ala Leu Glu Glu Ile Ser Thr Ile Cys
      20          25          30
Arg Ala Asp Val Leu
      35

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&lt;210&gt; 310

&lt;211&gt; 70

&lt;212&gt; PRT

&lt;213&gt; Mouse

<400> 310  
 Met Ala Ala Ser Trp Gly Gln Val Leu Ala Leu Val Leu Val Ala Ala  
 1 5 10 15  
 Leu Trp Gly Gly Thr Gln Pro Leu Leu Lys Arg Ala Ser Ser Gly Leu  
 20 25 30  
 Glu Gln Val Arg Glu Arg Thr Trp Ala Trp Gln Leu Leu Gln Glu Ile  
 35 40 45  
 Lys Ala Leu Phe Gly Asn Thr Glu Val Arg Leu Ala Leu Thr Asp Glu  
 50 55 60  
 Pro Leu Lys Ile Ser Pro  
 65 70

<210> 311  
 <211> 58  
 <212> PRT  
 <213> Human

<400> 311  
 Met Leu Leu Ser Ser Leu Val Ser Leu Ala Gly Ser Val Tyr Leu Ala  
 1 5 10 15  
 Trp Ile Leu Phe Phe Val Leu Tyr Asp Phe Cys Ile Val Cys Ile Thr  
 20 25 30  
 Thr Tyr Ala Ile Asn Val Ser Leu Met Trp Leu Ser Phe Arg Lys Val  
 35 40 45  
 Gln Glu Pro Gln Gly Lys Ala Lys Arg His  
 50 55

<210> 312  
 <211> 52  
 <212> PRT  
 <213> Human

<400> 312  
 Met Gly Thr Pro Gln Gly Glu Asn Trp Leu Ser Trp Met Phe Glu Lys  
 1 5 10 15  
 Leu Val Val Val Met Val Cys Tyr Phe Ile Leu Ser Ile Ile Asn Ser  
 20 25 30  
 Met Ala Gln Ser Tyr Ala Lys Arg Ile Gln Gln Arg Leu Asn Ser Glu  
 35 40 45  
 Glu Lys Thr Lys  
 50

<210> 313  
 <211> 70  
 <212> PRT  
 <213> Human

<400> 313  
 Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly Leu Met Leu Lys  
 1 5 10 15  
 Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser Phe Ile Ser Phe  
 20 25 30  
 Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met Met Ser Ser Phe  
 35 40 45  
 Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu Gln Asn Pro Gln  
 50 55 60  
 Pro Met Thr Pro Pro Trp  
 65 70

<210> 314  
 <211> 58

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 314

Met	Phe	Ile	Thr	Pro	Phe	Lys	Ala	Phe	Leu	Pro	Leu	Tyr	Leu	Leu	Thr
1				5					10					15	
Glu	Leu	Ser	Leu	Ile	Asp	Ile	Thr	Ser	Cys	Asp	Asp	Leu	Pro	His	Ser
			20					25					30		
Val	Leu	Pro	Gln	His	Leu	Ser	Phe	Glu	Phe	Val	Leu	Trp	Ser	Met	Tyr
		35					40					45			
Leu	Leu	Ile	Cys	Cys	Phe	Val	Ile	Ile	Phe						
		50					55								

&lt;210&gt; 315

&lt;211&gt; 229

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 315

Met	Ala	Ser	Ala	Leu	Glu	Glu	Leu	Gln	Lys	Asp	Leu	Glu	Glu	Val	Lys
1				5					10					15	
Val	Leu	Leu	Glu	Lys	Ser	Thr	Arg	Lys	Arg	Leu	Arg	Asp	Thr	Leu	Thr
			20					25					30		
Asn	Glu	Lys	Ser	Lys	Ile	Glu	Thr	Glu	Leu	Arg	Asn	Lys	Met	Gln	Gln
		35					40					45			
Lys	Ser	Gln	Lys	Lys	Pro	Glu	Phe	Asp	Asn	Glu	Lys	Pro	Ala	Ala	Val
		50				55					60				
Val	Ala	Pro	Leu	Thr	Thr	Gly	Tyr	Thr	Val	Lys	Ile	Ser	Asn	Tyr	Gly
65					70					75				80	
Trp	Asp	Gln	Ser	Asp	Lys	Phe	Val	Lys	Ile	Tyr	Ile	Thr	Leu	Thr	Gly
			85					90					95		
Val	His	Gln	Val	Pro	Ala	Glu	Asn	Val	Gln	Val	His	Phe	Thr	Glu	Arg
			100					105					110		
Ser	Phe	Asp	Leu	Leu	Val	Lys	Asn	Leu	Asn	Gly	Lys	Asn	Tyr	Ser	Met
		115					120					125			
Ile	Val	Asn	Asn	Leu	Leu	Lys	Pro	Ile	Ser	Val	Glu	Ser	Ser	Ser	Lys
		130				135					140				
Lys	Val	Lys	Thr	Asp	Thr	Val	Ile	Ile	Leu	Cys	Arg	Lys	Lys	Ala	Glu
145					150					155				160	
Asn	Thr	Arg	Trp	Asp	Tyr	Leu	Thr	Gln	Val	Glu	Lys	Glu	Cys	Lys	Glu
			165					170					175		
Lys	Glu	Lys	Pro	Ser	Tyr	Asp	Thr	Glu	Ala	Asp	Pro	Ser	Glu	Gly	Leu
			180					185					190		
Met	Asn	Val	Leu	Lys	Lys	Ile	Tyr	Glu	Asp	Gly	Asp	Asp	Asp	Met	Lys
		195				200						205			
Arg	Thr	Ile	Asn	Lys	Ala	Trp	Val	Glu	Ser	Arg	Glu	Lys	Gln	Ala	Arg
		210				215					220				
Glu	Asp	Thr	Glu	Phe											
225															

&lt;210&gt; 316

&lt;211&gt; 128

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 316

Arg	Ala	Glu	Phe	Gly	Thr	Ser	Gly	Glu	Met	Gly	Asn	Ala	Ala	Leu	Gly
1				5					10					15	
Ala	Glu	Leu	Gly	Val	Arg	Val	Leu	Leu	Phe	Val	Ala	Phe	Leu	Ala	Thr
			20					25					30		
Glu	Leu	Leu	Pro	Pro	Phe	Gln	Arg	Arg	Ile	Gln	Pro	Glu	Glu	Leu	Trp

35 40 45  
 Leu Tyr Arg Asn Pro Tyr Val Glu Ala Glu Tyr Phe Pro Thr Gly Pro  
 50 55 60  
 Met Phe Val Ile Ala Phe Leu Thr Pro Leu Ser Leu Ile Phe Phe Ala  
 65 70 75 80  
 Lys Phe Leu Arg Lys Ala Asp Ala Thr Asp Ser Lys Gln Ala Cys Leu  
 85 90 95  
 Ala Ala Ser Leu Ala Leu Ala Leu Asn Gly Val Phe Thr Asn Ile Ile  
 100 105 110  
 Lys Leu Ile Val Gly Arg Pro Arg Pro Asp Phe Phe Tyr Arg Cys Phe  
 115 120 125

&lt;210&gt; 317

&lt;211&gt; 75

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 317

Ser Ala Gly Val Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile  
 1 5 10 15  
 Ala Phe Gly Pro Ala Leu Ser Leu Tyr Val Phe Thr Ile Ala Thr Asp  
 20 25 30  
 Pro Leu Arg Val Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val  
 35 40 45  
 Ser Leu Leu Leu Ser Ser Val Phe Trp Phe Leu Val Arg Val Ile Thr  
 50 55 60  
 Asp Asn Arg Asp Gly Pro Val Gln Asn Tyr Leu  
 65 70 75

&lt;210&gt; 318

&lt;211&gt; 43

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 318

Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys  
 1 5 10 15  
 Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu  
 20 25 30  
 Ser Arg Thr Pro Arg Pro Thr Ala Leu Gly Asn  
 35 40

&lt;210&gt; 319

&lt;211&gt; 86

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 319

Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile  
 1 5 10 15  
 Cys Val Phe Trp Asp Phe Ile Phe Ile Phe Phe Asn Val Leu Ser  
 20 25 30  
 Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala  
 35 40 45  
 Gly Ala Gln Gly Met Trp Gly Ile Trp Gly His Thr Ile Thr Cys Gly  
 50 55 60  
 Leu Ala Pro Gly Ala Lys Pro Cys Ser Leu Lys Arg Glu Gly Pro Asp  
 65 70 75 80  
 Leu Leu Ser Phe Pro Pro  
 85

<210> 320  
 <211> 60  
 <212> PRT  
 <213> Mouse

<400> 320  
 Lys Gly Pro Glu Val Ser Cys Cys Ile Lys Tyr Phe Ile Phe Gly Phe  
 1 5 10 15  
 Asn Val Ile Phe Trp Phe Leu Gly Ile Thr Phe Leu Gly Ile Gly Leu  
 20 25 30  
 Trp Ala Trp Asn Glu Lys Gly Val Leu Ser Asn Ile Ser Ser Ile Thr  
 35 40 45  
 Asp Leu Gly Gly Phe Asp Pro Val Trp Leu Phe Leu  
 50 55 60

<210> 321  
 <211> 160  
 <212> PRT  
 <213> Mouse

<400> 321  
 Ile Arg His Glu Ala Glu Ala Gly Arg His Gln Pro Glu Gln Leu Ala  
 1 5 10 15  
 Ala Asp Ser Arg Thr Glu Thr Val Gly Pro Arg Gln Ser Asn Gly Leu  
 20 25 30  
 Thr Gly Pro Gly Leu Pro Thr Trp Gln Leu His Pro Val Leu Phe Pro  
 35 40 45  
 Glu Leu Val Leu Trp Val Asn Met Val Pro Cys Phe Leu Leu Ser Leu  
 50 55 60  
 Leu Leu Leu Val Arg Pro Ala Pro Val Val Ala Tyr Ser Val Ser Leu  
 65 70 75 80  
 Pro Ala Ser Phe Leu Glu Glu Val Ala Gly Ser Gly Glu Ala Glu Gly  
 85 90 95  
 Ser Ser Ala Ser Ser Pro Ser Leu Leu Pro Pro Arg Thr Pro Ala Phe  
 100 105 110  
 Ser Pro Thr Pro Gly Arg Thr Gln Pro Thr Ala Pro Val Gly Pro Val  
 115 120 125  
 Pro Pro Thr Asn Leu Leu Asp Gly Ile Val Asp Phe Phe Arg Gln Tyr  
 130 135 140  
 Val Met Leu Ile Ala Val Val Gly Ser Leu Thr Phe Leu Ile Ser Ser  
 145 150 155 160

<210> 322  
 <211> 54  
 <212> PRT  
 <213> Mouse

<400> 322  
 Arg Leu Gln Val Asp Thr Ser Gly Ser Lys Val Leu Phe Leu Phe Phe  
 1 5 10 15  
 Phe Phe Phe Leu Cys Val Cys Val Leu Val Cys Cys Cys Phe Gly Phe  
 20 25 30  
 Pro Gly Thr His Ser Val Asp Gln Ala Ser Pro Lys Leu Arg Asn Leu  
 35 40 45  
 Pro Pro Glu Cys Trp Asp  
 50

<210> 323  
 <211> 280  
 <212> PRT  
 <213> Mouse



&lt;400&gt; 323

Leu Asp Ser Arg Ala Cys Arg Ser Thr Leu Val Asp Pro Lys Asn Ser  
 1 5 10 15  
 Ala Arg Glu Asn Ile Arg Glu Tyr Val Arg Trp Met Met Tyr Trp Ile  
 20 25 30  
 Val Phe Ala Ile Phe Met Ala Ala Glu Thr Phe Thr Asp Ile Phe Ile  
 35 40 45  
 Ser Trp Ser Gly Pro Arg Ile Gly Arg Pro Trp Gly Trp Glu Gly Pro  
 50 55 60  
 His His His His His Leu Ala Ser Gly Ser His Lys Pro Leu Pro Leu  
 65 70 75 80  
 Leu Thr His Arg Phe Pro Phe Tyr Tyr Glu Phe Lys Met Ala Phe Val  
 85 90 95  
 Leu Trp Leu Leu Ser Pro Tyr Thr Lys Gly Ala Ser Leu Leu Tyr Arg  
 100 105 110  
 Lys Phe Val His Pro Ser Leu Ser Arg His Glu Lys Glu Ile Asp Ala  
 115 120 125  
 Cys Ile Val Gln Ala Lys Glu Arg Ser Tyr Glu Thr Met Leu Ser Phe  
 130 135 140  
 Gly Lys Arg Ser Leu Asn Ile Ala Ala Ser Ala Ala Val Gln Ala Ala  
 145 150 155 160  
 Thr Lys Ser Gln Gly Ala Leu Ala Gly Arg Leu Arg Ser Phe Ser Met  
 165 170 175  
 Gln Asp Leu Arg Ser Ile Pro Asp Thr Pro Val Pro Thr Tyr Gln Asp  
 180 185 190  
 Pro Leu Tyr Leu Glu Asp Gln Val Pro Arg Arg Arg Pro Pro Ile Gly  
 195 200 205  
 Tyr Arg Pro Gly Gly Leu Gln Gly Ser Asp Thr Glu Asp Glu Cys Trp  
 210 215 220  
 Ser Asp Asn Glu Ile Val Pro Gln Pro Pro Val Gly Pro Arg Glu Lys  
 225 230 235 240  
 Pro Leu Gly Arg Ser Gln Ser Leu Arg Val Val Lys Arg Lys Pro Leu  
 245 250 255  
 Thr Arg Glu Gly Thr Ser Arg Ser Leu Lys Val Arg Thr Pro Lys Lys  
 260 265 270  
 Ala Met Pro Ser Asp Met Asp Ser  
 275 280

&lt;210&gt; 324

&lt;211&gt; 166

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 324

Ala Leu Arg Arg Val Gly Met Glu Leu Pro Ala Val Asn Leu Lys Val  
 1 5 10 15  
 Ile Leu Leu Val His Trp Leu Leu Thr Thr Trp Gly Cys Leu Ala Phe  
 20 25 30  
 Ser Gly Ser Tyr Ala Trp Gly Asn Phe Thr Ile Leu Ala Leu Gly Val  
 35 40 45  
 Trp Ala Val Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu  
 50 55 60  
 Gly Gly Leu Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile  
 65 70 75 80  
 Phe Tyr Ser Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly  
 85 90 95  
 Met Ala Ile Phe Ser Leu Leu Leu Lys Pro Phe Ser Cys Cys Leu Val  
 100 105 110  
 Tyr His Met His Arg Glu Arg Gly Gly Glu Leu Pro Leu Arg Ser Asp  
 115 120 125

Phe Phe Gly Pro Ser Gln Glu His Ser Ala Tyr Gln Thr Ile Asp Ser  
 130 135 140  
 Ser Asp Ser Pro Ala Asp Pro Leu Ala Ser Leu Glu Asn Lys Gly Gln  
 145 150 155 160  
 Ala Ala Pro Arg Gly Tyr  
 165

&lt;210&gt; 325

&lt;211&gt; 338

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 325

Ile Arg His Glu Ala Glu Ala Gly Arg His Gln Pro Glu Gln Leu Ala  
 1 5 10 15  
 Ala Asp Ser Arg Thr Glu Thr Val Gly Pro Arg Gln Ser Asn Gly Leu  
 20 25 30  
 Thr Gly Pro Gly Leu Pro Thr Trp Gln Leu His Pro Val Leu Phe Pro  
 35 40 45  
 Glu Leu Val Leu Trp Val Asn Met Val Pro Cys Phe Leu Leu Ser Leu  
 50 55 60  
 Leu Leu Leu Val Arg Pro Ala Pro Val Val Ala Tyr Ser Val Ser Leu  
 65 70 75 80  
 Pro Ala Ser Phe Leu Glu Glu Val Ala Gly Ser Gly Glu Ala Glu Gly  
 85 90 95  
 Ser Ser Ala Ser Ser Pro Ser Leu Leu Pro Pro Arg Thr Pro Ala Phe  
 100 105 110  
 Ser Pro Thr Pro Gly Arg Thr Gln Pro Thr Ala Pro Val Gly Pro Val  
 115 120 125  
 Pro Pro Thr Asn Leu Leu Asp Gly Ile Val Asp Phe Phe Arg Gln Tyr  
 130 135 140  
 Val Met Leu Ile Ala Val Val Gly Ser Leu Thr Phe Leu Ile Met Phe  
 145 150 155 160  
 Ile Val Cys Ala Ala Leu Ile Thr Arg Gln Lys His Lys Ala Thr Ala  
 165 170 175  
 Tyr Tyr Pro Ser Ser Phe Pro Glu Lys Lys Tyr Val Asp Gln Arg Asp  
 180 185 190  
 Arg Ala Gly Gly Pro His Ala Phe Ser Glu Val Pro Asp Arg Ala Pro  
 195 200 205  
 Asp Ser Arg Gln Glu Glu Gly Leu Asp Ser Ser Gln Gln Leu Gln Ala  
 210 215 220  
 Asp Ile Leu Ala Ala Thr Gln Asn Leu Arg Ser Pro Ala Arg Ala Leu  
 225 230 235 240  
 Pro Gly Ser Gly Glu Gly Thr Lys Gln Val Lys Gly Gly Ser Glu Glu  
 245 250 255  
 Glu Glu Glu Lys Glu Glu Glu Val Phe Ser Gly Gln Glu Glu Pro Arg  
 260 265 270  
 Glu Ala Pro Val Cys Gly Val Thr Glu Glu Lys Pro Glu Val Pro Asp  
 275 280 285  
 Glu Thr Ala Ser Ala Glu Ala Glu Gly Val Pro Ala Ala Ser Glu Gly  
 290 295 300  
 Gln Gly Glu Pro Glu Gly Ser Phe Ser Leu Ala Gln Glu Pro Gln Gly  
 305 310 315 320  
 Ala Ala Gly Pro Ser Glu Arg Ser Cys Ala Cys Asn Arg Ile Ser Pro  
 325 330 335  
 Asn Val

&lt;210&gt; 326

&lt;211&gt; 347

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 326

Ala Trp Ser Arg Pro Arg Tyr Tyr Arg Leu Cys Asp Lys Ala Glu Ala  
 1 5 10 15  
 Trp Gly Ile Val Leu Glu Thr Val Ala Thr Ala Gly Val Val Thr Ser  
 20 25 30  
 Val Ala Phe Met Leu Thr Leu Pro Ile Leu Val Cys Lys Val Gln Asp  
 35 40 45  
 Ser Asn Arg Arg Lys Met Leu Pro Thr Gln Phe Leu Phe Leu Leu Gly  
 50 55 60  
 Val Leu Gly Ile Phe Gly Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp  
 65 70 75 80  
 Gly Ser Thr Gly Pro Thr Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser  
 85 90 95  
 Ile Cys Phe Ser Cys Leu Leu Ala His Ala Val Ser Leu Thr Lys Leu  
 100 105 110  
 Val Arg Gly Arg Lys Pro Leu Ser Leu Leu Val Ile Leu Gly Leu Ala  
 115 120 125  
 Val Gly Phe Ser Leu Val Gln Asp Val Ile Ala Ile Glu Tyr Ile Val  
 130 135 140  
 Leu Thr Met Asn Arg Thr Asn Val Asn Val Phe Ser Glu Leu Ser Ala  
 145 150 155 160  
 Pro Arg Arg Asn Glu Asp Phe Val Leu Leu Leu Thr Tyr Val Leu Phe  
 165 170 175  
 Leu Met Ala Leu Thr Phe Leu Met Ser Ser Phe Thr Phe Cys Gly Ser  
 180 185 190  
 Phe Thr Gly Trp Lys Arg His Gly Ala His Ile Tyr Leu Thr Met Leu  
 195 200 205  
 Leu Ser Ile Ala Ile Trp Val Ala Trp Ile Thr Leu Leu Met Leu Pro  
 210 215 220  
 Asp Phe Asp Arg Arg Trp Asp Asp Thr Ile Leu Ser Ser Ala Leu Ala  
 225 230 235 240  
 Ala Asn Gly Trp Val Phe Leu Leu Ala Tyr Val Ser Pro Glu Phe Trp  
 245 250 255  
 Leu Leu Thr Lys Gln Arg Asn Pro Met Asp Tyr Pro Val Glu Asp Ala  
 260 265 270  
 Phe Cys Lys Pro Gln Leu Val Lys Lys Ser Tyr Gly Val Glu Asn Arg  
 275 280 285  
 Ala Tyr Ser Gln Glu Glu Ile Thr Gln Gly Phe Glu Glu Thr Gly Asp  
 290 295 300  
 Thr Leu Tyr Ala Pro Tyr Ser Thr His Phe Gln Leu Gln Asn Gln Pro  
 305 310 315 320  
 Pro Gln Lys Glu Phe Ser Ile Pro Arg Ala His Ala Trp Pro Ser Pro  
 325 330 335  
 Tyr Lys Asp Tyr Glu Val Lys Lys Glu Gly Ser  
 340 345

&lt;210&gt; 327

&lt;211&gt; 141

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 327

Lys Asn Ser Lys Cys Leu Leu Phe Trp Cys Arg Lys Ile Val Gly Asn  
 1 5 10 15  
 Arg Gln Glu Pro Met Trp Glu Phe Asn Phe Lys Phe Lys Lys Gln Ser  
 20 25 30  
 Pro Arg Leu Lys Ser Lys Cys Thr Gly Gly Leu Gln Pro Pro Val Gln  
 35 40 45  
 Tyr Glu Asp Val His Thr Asn Pro Asp Gln Asp Cys Cys Leu Leu Gln

50 55 60  
 Val Thr Thr Leu Asn Phe Ile Phe Ile Pro Ile Val Met Gly Met Ile  
 65 70 75 80  
 Phe Thr Leu Phe Thr Ile Asn Val Ser Thr Asp Met Arg His His Arg  
 85 90 95  
 Val Arg Leu Val Phe Gln Asp Ser Pro Val His Gly Gly Arg Lys Leu  
 100 105 110  
 Arg Ser Glu Gln Gly Val Gln Val Ile Leu Asp Gln Cys Thr Ala Phe  
 115 120 125  
 Gly Ser Leu Thr Gly Gly Ile Leu Ser Thr His Ser Pro  
 130 135 140

&lt;210&gt; 328

&lt;211&gt; 71

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 328

Arg Glu Arg Thr Ser Leu Glu Phe Phe Val Phe Leu Phe Leu Phe Ile  
 1 5 10 15  
 Cys Cys Cys Leu His Ser Gly Gly Leu Gly Gly Val Pro Leu Pro Pro  
 20 25 30  
 Phe Pro Pro Gln Ala Gln Arg Gly Glu Gly Pro Gly Lys Trp Met Ser  
 35 40 45  
 Pro Pro Leu Pro Pro His Pro Val Val Ala Pro Pro Thr Pro Ser Pro  
 50 55 60  
 Ser Arg Gly Cys Val Leu Leu  
 65 70

&lt;210&gt; 329

&lt;211&gt; 109

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 329

Asp Gly Pro Ser Pro Lys Leu Ala Leu Trp Leu Pro Ser Pro Ala Pro  
 1 5 10 15  
 Thr Ala Ala Pro Thr Ala Leu Gly Glu Ala Gly Leu Ala Glu His Ser  
 20 25 30  
 Gln Arg Asp Asp Arg Trp Leu Leu Val Ala Leu Leu Val Pro Thr Cys  
 35 40 45  
 Val Phe Leu Val Val Leu Leu Ala Leu Gly Ile Val Tyr Cys Thr Arg  
 50 55 60  
 Cys Gly Pro His Ala Pro Asn Lys Arg Ile Thr Asp Cys Tyr Arg Trp  
 65 70 75 80  
 Val Ile His Ala Gly Ser Lys Ser Pro Thr Glu Pro Met Pro Pro Arg  
 85 90 95  
 Gly Ser Leu Thr Gly Val Gln Thr Cys Arg Thr Ser Val  
 100 105

&lt;210&gt; 330

&lt;211&gt; 155

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 330

Ser Val Met Ala Ala Gly Leu Phe Gly Leu Ser Ala Arg Arg Leu Leu  
 1 5 10 15  
 Ala Ala Ala Ala Thr Arg Gly Leu Pro Ala Ala Arg Val Arg Trp Glu  
 20 25 30  
 Ser Ser Phe Ser Arg Thr Val Val Ala Pro Ser Ala Val Ala Gly Lys

35 40 45  
 Arg Pro Pro Glu Pro Thr Thr Pro Trp Gln Glu Asp Pro Glu Pro Glu  
 50 55 60  
 Asp Glu Asn Leu Tyr Glu Lys Asn Pro Asp Ser His Gly Tyr Asp Lys  
 65 70 75 80  
 Asp Pro Val Leu Asp Val Trp Asn Met Arg Leu Val Phe Phe Phe Gly  
 85 90 95  
 Val Ser Ile Ile Leu Val Leu Gly Ser Thr Phe Val Ala Tyr Leu Pro  
 100 105 110  
 Asp Tyr Arg Met Lys Glu Trp Ser Arg Arg Glu Ala Glu Arg Leu Val  
 115 120 125  
 Lys Tyr Arg Glu Ala Asn Gly Leu Pro Ile Met Glu Ser Asn Cys Phe  
 130 135 140  
 Asp Pro Ser Lys Ile Gln Leu Pro Glu Asp Glu  
 145 150 155

<210> 331  
 <211> 299  
 <212> PRT  
 <213> Human

<400> 331  
 Met Gly Thr Lys Ala Gln Val Glu Arg Lys Leu Leu Cys Leu Phe Ile  
 1 5 10 15  
 Leu Ala Ile Leu Leu Cys Ser Leu Ala Leu Gly Ser Val Thr Val His  
 20 25 30  
 Ser Ser Glu Pro Glu Val Arg Ile Pro Glu Asn Asn Pro Val Lys Leu  
 35 40 45  
 Ser Cys Ala Tyr Ser Gly Phe Ser Ser Pro Arg Val Glu Trp Lys Phe  
 50 55 60  
 Asp Gln Gly Asp Thr Thr Arg Leu Val Cys Tyr Asn Asn Lys Ile Thr  
 65 70 75 80  
 Ala Ser Tyr Glu Asp Arg Val Thr Phe Leu Pro Thr Gly Ile Thr Phe  
 85 90 95  
 Lys Ser Val Thr Arg Glu Asp Thr Gly Thr Tyr Thr Cys Met Val Ser  
 100 105 110  
 Glu Glu Gly Gly Asn Ser Tyr Gly Glu Val Lys Val Lys Leu Ile Val  
 115 120 125  
 Leu Val Pro Pro Ser Lys Pro Thr Val Asn Ile Pro Ser Ser Ala Thr  
 130 135 140  
 Ile Gly Asn Arg Ala Val Leu Thr Cys Ser Glu Gln Asp Gly Ser Pro  
 145 150 155 160  
 Pro Ser Glu Tyr Thr Trp Phe Lys Asp Gly Ile Val Met Pro Thr Asn  
 165 170 175  
 Pro Lys Ser Thr Arg Ala Phe Ser Asn Ser Ser Tyr Val Leu Asn Pro  
 180 185 190  
 Thr Thr Gly Glu Leu Val Phe Asp Pro Leu Ser Ala Ser Asp Thr Gly  
 195 200 205  
 Glu Tyr Ser Cys Glu Ala Arg Asn Gly Tyr Gly Thr Pro Met Thr Ser  
 210 215 220  
 Asn Ala Val Arg Met Glu Ala Val Glu Arg Asn Val Gly Val Ile Val  
 225 230 235 240  
 Ala Ala Val Leu Val Thr Leu Ile Leu Leu Gly Ile Leu Val Phe Gly  
 245 250 255  
 Ile Trp Phe Ala Tyr Ser Arg Gly His Phe Asp Arg Thr Lys Lys Gly  
 260 265 270  
 Thr Ser Ser Lys Lys Val Ile Tyr Ser Gln Pro Ser Ala Arg Ser Glu  
 275 280 285  
 Gly Glu Phe Lys Gln Thr Ser Ser Phe Leu Val  
 290 295

<210> 332  
 <211> 299  
 <212> PRT  
 <213> Mouse

<400> 332  
 Ala Arg Ala Gly Ala Cys Tyr Cys Pro Ala Gly Phe Leu Gly Ala Asp  
 1 5 10 15  
 Cys Ser Leu Ala Cys Pro Gln Gly Arg Phe Gly Pro Ser Cys Ala His  
 20 25 30  
 Val Cys Thr Cys Gly Gln Gly Ala Ala Cys Asp Pro Val Ser Gly Thr  
 35 40 45  
 Cys Ile Cys Pro Pro Gly Lys Thr Gly Gly His Cys Glu Arg Gly Cys  
 50 55 60  
 Pro Gln Asp Arg Phe Gly Lys Gly Cys Glu His Lys Cys Ala Cys Arg  
 65 70 75 80  
 Asn Gly Gly Leu Cys His Ala Thr Asn Gly Ser Cys Ser Cys Pro Leu  
 85 90 95  
 Gly Trp Met Gly Pro His Cys Glu His Ala Cys Pro Ala Gly Arg Tyr  
 100 105 110  
 Gly Ala Ala Cys Leu Leu Glu Cys Ser Cys Gln Asn Asn Gly Ser Cys  
 115 120 125  
 Glu Pro Thr Ser Gly Ala Cys Leu Cys Gly Pro Gly Phe Tyr Gly Gln  
 130 135 140  
 Ala Cys Glu Asp Thr Cys Pro Ala Gly Phe His Gly Ser Gly Cys Gln  
 145 150 155 160  
 Arg Val Cys Glu Cys Gln Gln Gly Ala Pro Cys Asp Pro Val Ser Gly  
 165 170 175  
 Arg Cys Leu Cys Pro Ala Gly Phe Arg Gly Gln Phe Cys Glu Arg Gly  
 180 185 190  
 Cys Lys Pro Gly Phe Phe Gly Asp Gly Cys Leu Gln Gln Cys Asn Cys  
 195 200 205  
 Pro Thr Gly Val Pro Cys Asp Pro Ile Ser Gly Leu Cys Leu Cys Pro  
 210 215 220  
 Pro Gly Arg Ala Gly Thr Thr Cys Asp Leu Asp Cys Arg Arg Gly Arg  
 225 230 235 240  
 Phe Gly Pro Gly Cys Ala Leu Arg Cys Asp Cys Gly Gly Gly Ala Asp  
 245 250 255  
 Cys Asp Pro Ile Ser Gly Gln Cys His Cys Val Asp Ser Tyr Thr Gly  
 260 265 270  
 Pro Thr Cys Arg Glu Val Pro Thr Gln Leu Ser Ser Ile Arg Pro Ala  
 275 280 285  
 Pro Gln His Ser Ser Ser Lys Ala Met Lys His  
 290 295

<210> 333  
 <211> 109  
 <212> PRT  
 <213> Mouse

<400> 333  
 Gly Thr Arg Val Gly Thr Pro Tyr Tyr Met Ser Pro Glu Arg Ile His  
 1 5 10 15  
 Glu Asn Gly Tyr Asn Phe Lys Ser Asp Ile Trp Ser Leu Gly Cys Leu  
 20 25 30  
 Leu Tyr Glu Met Ala Ala Leu Gln Ser Pro Phe Tyr Gly Asp Lys Met  
 35 40 45  
 Asn Leu Tyr Ser Leu Cys Lys Lys Ile Glu Gln Cys Asp Tyr Pro Pro  
 50 55 60  
 Leu Pro Ser Asp His Tyr Ser Glu Glu Leu Arg Gln Leu Val Asn Ile  
 65 70 75 80

Cys Ile Asn Pro Asp Pro Glu Lys Arg Pro Asp Ile Ala Tyr Val Tyr  
                             85                            90                            95  
 Asp Val Ala Lys Arg Met His Ala Cys Thr Ala Ser Thr  
                             100                            105

<210> 334  
 <211> 787  
 <212> PRT  
 <213> Mouse

<400> 334  
 Lys Val Glu Gly Glu Gly Arg Gly Arg Trp Ala Leu Gly Leu Leu Arg  
   1                            5                            10                            15  
 Thr Phe Asp Ala Gly Glu Phe Ala Gly Trp Glu Lys Val Gly Ser Gly  
                             20                            25                            30  
 Gly Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp  
                             35                            40                            45  
 Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg  
   50                            55                            60  
 Met Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg  
  65                            70                            75                            80  
 Tyr Ile Leu Pro Val Tyr Gly Ile Cys Gln Glu Pro Val Gly Leu Val  
                             85                            90                            95  
 Met Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu  
                             100                            105                            110  
 Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val  
                             115                            120                            125  
 Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp  
  130                            135                            140  
 Leu Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr His Val Lys Ile  
  145                            150                            155                            160  
 Ser Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His Asp  
                             165                            170                            175  
 Leu Ser Met Asp Gly Leu Phe Gly Thr Ile Ala Tyr Leu Pro Pro Glu  
                             180                            185                            190  
 Arg Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val Tyr  
                             195                            200                            205  
 Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Lys Lys Pro Phe  
  210                            215                            220  
 Ala Asp Glu Lys Asn Ile Leu His Ile Met Met Lys Val Val Lys Gly  
  225                            230                            235                            240  
 His Arg Pro Glu Leu Pro Pro Ile Cys Arg Pro Arg Pro Arg Ala Cys  
                             245                            250                            255  
 Ala Ser Leu Ile Gly Leu Met Gln Arg Cys Trp His Ala Asp Pro Gln  
                             260                            265                            270  
 Val Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu Cys  
                             275                            280                            285  
 Glu Lys Pro Asp Glu Glu Val Lys Asp Leu Ala His Glu Pro Gly Glu  
  290                            295                            300  
 Lys Ser Ser Leu Glu Ser Lys Ser Glu Ala Arg Pro Glu Ser Ser Arg  
  305                            310                            315                            320  
 Leu Lys Arg Ala Ser Ala Pro Pro Phe Asp Asn Asp Cys Ser Leu Ser  
                             325                            330                            335  
 Glu Leu Leu Ser Gln Leu Asp Ser Gly Ile Ser Gln Thr Leu Glu Gly  
                             340                            345                            350  
 Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Cys Lys Leu Pro Ser Ser  
                             355                            360                            365  
 Ser Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser Ala Phe  
  370                            375                            380  
 Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg Glu Ala Ser Thr  
  385                            390                            395                            400

Gly Asp Leu Gly Pro Thr Asp Ile Gln Lys Lys Lys Leu Val Asp Ala  
 405 410 415  
 Ile Ile Ser Gly Asp Thr Ser Arg Leu Met Lys Ile Leu Gln Pro Gln  
 420 425 430  
 Asp Val Asp Leu Val Leu Asp Ser Ser Ala Ser Leu Leu His Leu Ala  
 435 440 445  
 Val Glu Ala Gly Gln Glu Glu Cys Val Lys Trp Leu Leu Leu Asn Asn  
 450 455 460  
 Ala Asn Pro Asn Leu Thr Asn Arg Lys Gly Ser Thr Pro Leu His Met  
 465 470 475 480  
 Ala Val Glu Arg Lys Gly Arg Gly Ile Val Glu Leu Leu Leu Ala Arg  
 485 490 495  
 Lys Thr Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Ala Leu His  
 500 505 510  
 Phe Ala Ala Gln Asn Gly Asp Glu Ala Ser Thr Arg Leu Leu Leu Glu  
 515 520 525  
 Lys Asn Ala Ser Val Asn Glu Val Asp Phe Glu Gly Arg Thr Pro Met  
 530 535 540  
 His Val Ala Cys Gln His Gly Gln Glu Asn Ile Val Arg Thr Leu Leu  
 545 550 555 560  
 Arg Arg Gly Val Asp Val Gly Leu Gln Gly Lys Asp Ala Trp Leu Pro  
 565 570 575  
 Leu His Tyr Ala Ala Trp Gln Gly His Leu Pro Ile Val Lys Leu Leu  
 580 585 590  
 Ala Lys Gln Pro Gly Val Ser Val Asn Ala Gln Thr Leu Asp Gly Arg  
 595 600 605  
 Thr Pro Leu His Leu Ala Ala Gln Arg Gly His Tyr Arg Val Ala Arg  
 610 615 620  
 Ile Leu Ile Asp Leu Cys Ser Asp Val Asn Ile Cys Ser Leu Gln Ala  
 625 630 635 640  
 Gln Thr Pro Leu His Val Ala Ala Glu Thr Gly His Thr Ser Thr Ala  
 645 650 655  
 Arg Leu Leu Leu His Arg Gly Ala Gly Lys Glu Ala Leu Thr Ser Glu  
 660 665 670  
 Gly Tyr Thr Ala Leu His Leu Ala Ala Gln Asn Gly His Leu Ala Thr  
 675 680 685  
 Val Lys Leu Leu Ile Glu Glu Lys Ala Asp Val Met Ala Arg Gly Pro  
 690 695 700  
 Leu Asn Gln Thr Ala Leu His Leu Ala Ala Ala Arg Gly His Ser Glu  
 705 710 715 720  
 Val Val Glu Glu Leu Val Ser Ala Asp Leu Ile Asp Leu Ser Asp Glu  
 725 730 735  
 Gln Gly Leu Ser Ala Leu His Leu Ala Ala Gln Gly Arg His Ser Gln  
 740 745 750  
 Thr Val Glu Thr Leu Leu Lys His Gly Ala His Ile Asn Leu Gln Ser  
 755 760 765  
 Leu Lys Phe Gln Gly Gly Gln Ser Ser Ala Ala Thr Leu Leu Arg Arg  
 770 775 780  
 Ser Lys Thr  
 785

<210> 335  
 <211> 194  
 <212> PRT  
 <213> Mouse

<400> 335  
 Pro Gly Cys Lys Ser Cys Thr Val Cys Arg His Gly Leu Cys Arg Ser  
 1 5 10 15  
 Val Glu Lys Asp Ser Val Val Cys Glu Cys His Pro Gly Trp Thr Gly  
 20 25 30



Pro Leu Cys Asp Gln Glu Ala Arg Asp Pro Cys Leu Gly His Ser Cys  
 35 40 45  
 Arg His Gly Thr Cys Met Ala Thr Gly Asp Ser Tyr Val Cys Lys Cys  
 50 55 60  
 Ala Glu Gly Tyr Gly Gly Ala Leu Cys Asp Gln Lys Asn Asp Ser Ala  
 65 70 75 80  
 Ser Ala Cys Ser Ala Phe Lys Cys His His Gly Gln Cys His Ile Ser  
 85 90 95  
 Asp Arg Gly Glu Pro Tyr Cys Leu Cys Gln Pro Gly Phe Ser Gly His  
 100 105 110  
 His Cys Glu Gln Glu Asn Pro Cys Met Gly Glu Ile Val Arg Glu Ala  
 115 120 125  
 Ile Arg Arg Gln Lys Asp Tyr Ala Ser Cys Ala Thr Ala Ser Lys Val  
 130 135 140  
 Pro Ile Met Glu Cys Arg Gly Gly Cys Gly Thr Cys Cys Gln Pro  
 145 150 155 160  
 Ile Arg Ser Lys Arg Arg Lys Tyr Val Phe Gln Cys Thr Asp Gly Ser  
 165 170 175  
 Ser Phe Val Glu Glu Val Glu Arg His Leu Glu Cys Gly Cys Arg Ala  
 180 185 190  
 Cys Ser

<210> 336  
 <211> 274  
 <212> PRT  
 <213> Human

<400> 336  
 Tyr Arg Tyr Cys Gln His Arg Cys Val Asn Leu Pro Gly Ser Phe Arg  
 1 5 10 15  
 Cys Gln Cys Glu Pro Gly Phe Gln Leu Gly Pro Asn Asn Arg Ser Cys  
 20 25 30  
 Val Asp Val Asn Glu Cys Asp Met Gly Ala Pro Cys Glu Gln Arg Cys  
 35 40 45  
 Phe Asn Ser Tyr Gly Thr Phe Leu Cys Arg Cys His Gln Gly Tyr Glu  
 50 55 60  
 Leu His Arg Asp Gly Phe Ser Cys Ser Asp Ile Asp Glu Cys Ser Tyr  
 65 70 75 80  
 Ser Ser Tyr Leu Cys Gln Tyr Arg Cys Val Asn Glu Pro Gly Arg Phe  
 85 90 95  
 Ser Cys His Cys Pro Gln Gly Tyr Gln Leu Leu Ala Thr Arg Leu Cys  
 100 105 110  
 Gln Asp Ile Asp Glu Cys Glu Ser Gly Ala His Gln Cys Ser Glu Ala  
 115 120 125  
 Gln Thr Cys Val Asn Phe His Gly Gly Tyr Arg Cys Val Asp Thr Asn  
 130 135 140  
 Arg Cys Val Glu Pro Tyr Ile Gln Val Ser Glu Asn Arg Cys Leu Cys  
 145 150 155 160  
 Pro Ala Ser Asn Pro Leu Cys Arg Glu Gln Pro Ser Ser Ile Val His  
 165 170 175  
 Arg Tyr Met Thr Ile Thr Ser Glu Arg Ser Val Pro Ala Asp Val Phe  
 180 185 190  
 Gln Ile Gln Ala Thr Ser Val Tyr Pro Gly Ala Tyr Asn Ala Phe Gln  
 195 200 205  
 Ile Arg Ala Gly Asn Ser Gln Gly Asp Phe Tyr Ile Arg Gln Ile Asn  
 210 215 220  
 Asn Val Ser Ala Met Leu Val Leu Ala Arg Pro Val Thr Gly Pro Arg  
 225 230 235 240  
 Glu Tyr Val Leu Asp Leu Glu Met Val Thr Met Asn Ser Leu Met Ser  
 245 250 255

Tyr Arg Ala Ser Ser Val Leu Arg Leu Thr Val Phe Val Gly Ala Tyr  
 260 265 270  
 Thr Phe

<210> 337  
 <211> 316  
 <212> PRT  
 <213> Mouse

<400> 337  
 His Glu Glu Glu Pro Cys Asn Asn Gly Ser Glu Ile Leu Ala Tyr Asn  
 1 5 10 15  
 Ile Asp Leu Gly Asp Ser Cys Ile Thr Val Gly Asn Thr Thr His  
 20 25 30  
 Val Met Lys Asn Leu Leu Pro Glu Thr Thr Tyr Arg Ile Arg Ile Gln  
 35 40 45  
 Ala Ile Asn Glu Ile Gly Val Gly Pro Phe Ser Gln Phe Ile Lys Ala  
 50 55 60  
 Lys Thr Arg Pro Leu Pro Pro Ser Pro Pro Arg Leu Glu Cys Ala Ala  
 65 70 75 80  
 Ser Gly Pro Gln Ser Leu Lys Leu Lys Trp Gly Asp Ser Asn Ser Lys  
 85 90 95  
 Thr His Ala Ala Gly Asp Met Val Tyr Thr Leu Gln Leu Glu Asp Arg  
 100 105 110  
 Asn Lys Arg Phe Ile Ser Ile Tyr Arg Gly Pro Ser His Thr Tyr Lys  
 115 120 125  
 Val Gln Arg Leu Thr Glu Phe Thr Cys Tyr Ser Phe Arg Ile Gln Ala  
 130 135 140  
 Met Ser Glu Ala Gly Glu Gly Pro Tyr Ser Glu Thr Tyr Thr Phe Ser  
 145 150 155 160  
 Thr Thr Lys Ser Val Pro Pro Thr Leu Lys Ala Pro Arg Val Thr Gln  
 165 170 175  
 Leu Glu Gly Asn Ser Cys Glu Ile Phe Trp Glu Thr Val Pro Pro Met  
 180 185 190  
 Arg Gly Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp  
 195 200 205  
 Ser Glu Tyr Lys Gln Val Tyr Lys Gly Glu Glu Ala Thr Phe Gln Ile  
 210 215 220  
 Ser Gly Leu Gln Ser Asn Thr Asp Tyr Arg Phe Arg Val Cys Ala Cys  
 225 230 235 240  
 Arg Arg Cys Val Asp Thr Ser Gln Glu Leu Ser Gly Ala Phe Ser Pro  
 245 250 255  
 Ser Ala Ala Phe Met Leu Gln Gln Arg Glu Val Met Leu Thr Gly Asp  
 260 265 270  
 Leu Gly Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp  
 275 280 285  
 Glu Gln Phe Ala Ala Leu Ile Val Leu Gly Phe Ala Thr Leu Ser Ile  
 290 295 300  
 Leu Phe Ala Phe Ile Leu Gln Tyr Phe Leu Met Lys  
 305 310 315

<210> 338  
 <211> 237  
 <212> PRT  
 <213> Mouse

<400> 338  
 Met Leu Ser Leu Arg Ser Leu Leu Pro His Leu Gly Leu Phe Leu Cys  
 1 5 10 15  
 Leu Ala Leu His Leu Ser Pro Ser Leu Ser Ala Ser Asp Asn Gly Ser

	20		25		30										
Cys	Val	Val	Leu	Asp	Asn	Ile	Tyr	Thr	Ser	Asp	Ile	Leu	Glu	Ile	Ser
	35						40					45			
Thr	Met	Ala	Asn	Val	Ser	Gly	Gly	Asp	Val	Thr	Tyr	Thr	Val	Thr	Val
	50					55					60				
Pro	Val	Asn	Asp	Ser	Val	Ser	Ala	Val	Ile	Leu	Lys	Ala	Val	Lys	Glu
65					70					75					80
Asp	Asp	Ser	Pro	Val	Gly	Thr	Trp	Ser	Gly	Thr	Tyr	Glu	Lys	Cys	Asn
			85						90					95	
Asp	Ser	Ser	Val	Tyr	Tyr	Asn	Leu	Thr	Ser	Gln	Ser	Gln	Ser	Val	Phe
	100							105					110		
Gln	Thr	Asn	Trp	Thr	Val	Pro	Thr	Ser	Glu	Asp	Val	Thr	Lys	Val	Asn
	115						120					125			
Leu	Gln	Val	Leu	Ile	Val	Val	Asn	Arg	Thr	Ala	Ser	Lys	Ser	Ser	Val
	130					135					140				
Lys	Met	Glu	Gln	Val	Gln	Pro	Ser	Ala	Ser	Thr	Pro	Ile	Pro	Glu	Ser
145					150					155					160
Ser	Glu	Thr	Ser	Gln	Thr	Ile	Asn	Thr	Thr	Pro	Thr	Val	Asn	Thr	Ala
			165					170						175	
Lys	Thr	Thr	Ala	Lys	Asp	Thr	Ala	Asn	Thr	Thr	Ala	Val	Thr	Thr	Ala
	180						185						190		
Asn	Thr	Thr	Ala	Asn	Thr	Thr	Ala	Val	Thr	Thr	Ala	Lys	Thr	Thr	Ala
	195						200					205			
Lys	Ser	Leu	Ala	Ile	Arg	Thr	Leu	Gly	Ser	Pro	Leu	Ala	Gly	Ala	Leu
	210					215					220				
His	Ile	Leu	Leu	Val	Phe	Leu	Ile	Ser	Lys	Leu	Leu	Phe			
225					230					235					

&lt;210&gt; 339

&lt;211&gt; 469

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 339

Met	Leu	Cys	Leu	Cys	Leu	Tyr	Val	Pro	Ile	Ala	Gly	Ala	Ala	Gln	Thr
1			5					10						15	
Glu	Phe	Gln	Tyr	Phe	Glu	Ser	Lys	Gly	Leu	Pro	Ala	Glu	Leu	Lys	Ser
		20						25					30		
Ile	Phe	Lys	Leu	Ser	Val	Phe	Ile	Pro	Ser	Gln	Glu	Phe	Ser	Thr	Tyr
	35					40						45			
Arg	Gln	Trp	Lys	Gln	Lys	Ile	Val	Gln	Ala	Gly	Asp	Lys	Asp	Leu	Asp
	50				55						60				
Gly	Gln	Leu	Asp	Phe	Glu	Glu	Phe	Val	His	Tyr	Leu	Gln	Asp	His	Glu
65					70					75					80
Lys	Lys	Leu	Arg	Leu	Val	Phe	Lys	Ser	Leu	Asp	Lys	Lys	Asn	Asp	Gly
			85					90					95		
Arg	Ile	Asp	Ala	Gln	Glu	Ile	Met	Gln	Ser	Leu	Arg	Asp	Leu	Gly	Val
	100							105					110		
Lys	Ile	Ser	Glu	Gln	Gln	Ala	Glu	Lys	Ile	Leu	Lys	Ser	Met	Asp	Lys
	115						120					125			
Asn	Gly	Thr	Met	Thr	Ile	Asp	Trp	Asn	Glu	Trp	Arg	Asp	Tyr	His	Leu
	130					135					140				
Leu	His	Pro	Val	Glu	Asn	Ile	Pro	Glu	Ile	Ile	Leu	Tyr	Trp	Lys	His
145					150					155					160
Ser	Thr	Ile	Phe	Asp	Val	Gly	Glu	Asn	Leu	Thr	Val	Pro	Asp	Glu	Phe
			165					170						175	
Thr	Val	Glu	Glu	Arg	Gln	Thr	Gly	Met	Trp	Trp	Arg	His	Leu	Val	Ala
	180						185						190		
Gly	Gly	Gly	Ala	Gly	Ala	Val	Ser	Arg	Thr	Cys	Thr	Ala	Pro	Leu	Asp
	195					200						205			
Arg	Leu	Lys	Val	Leu	Met	Gln	Val	His	Ala	Ser	Arg	Ser	Asn	Asn	Met

210 215 220  
 Cys Ile Val Gly Gly Phe Thr Gln Met Ile Arg Glu Gly Gly Ala Lys  
 225 230 235 240  
 Ser Leu Trp Arg Gly Asn Gly Ile Asn Val Leu Lys Ile Ala Pro Glu  
 245 250 255  
 Ser Ala Ile Lys Phe Met Ala Tyr Glu Gln Met Lys Arg Leu Val Gly  
 260 265 270  
 Ser Asp Gln Glu Thr Leu Arg Ile His Glu Arg Leu Val Ala Gly Ser  
 275 280 285  
 Leu Ala Gly Ala Ile Ala Gln Ser Ser Ile Tyr Pro Met Glu Val Leu  
 290 295 300  
 Lys Thr Arg Met Ala Leu Arg Lys Thr Gly Gln Tyr Ser Gly Met Leu  
 305 310 315 320  
 Asp Cys Ala Arg Arg Ile Leu Ala Lys Glu Gly Val Ala Ala Phe Tyr  
 325 330 335  
 Lys Gly Tyr Ile Pro Asn Met Leu Gly Ile Ile Pro Tyr Ala Gly Ile  
 340 345 350  
 Asp Leu Ala Val Tyr Glu Thr Leu Lys Asn Thr Trp Leu Gln Arg Tyr  
 355 360 365  
 Ala Val Asn Ser Ala Asp Pro Gly Val Phe Val Leu Leu Ala Cys Gly  
 370 375 380  
 Thr Ile Ser Ser Thr Cys Gly Gln Leu Ala Ser Tyr Pro Leu Ala Leu  
 385 390 395 400  
 Val Arg Thr Arg Met Gln Ala Gln Ala Ser Ile Glu Gly Ala Pro Glu  
 405 410 415  
 Val Thr Met Ser Ser Leu Phe Lys Gln Ile Leu Arg Thr Glu Gly Ala  
 420 425 430  
 Phe Gly Leu Tyr Arg Gly Leu Ala Pro Asn Phe Met Lys Val Ile Pro  
 435 440 445  
 Ala Val Ser Ile Ser Tyr Val Val Tyr Glu Asn Leu Lys Ile Thr Leu  
 450 455 460  
 Gly Val Gln Ser Arg  
 465

<210> 340  
 <211> 99  
 <212> PRT  
 <213> Mouse

<400> 340  
 Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Leu Ala Leu Cys  
 1 5 10 15  
 Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro  
 20 25 30  
 Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr  
 35 40 45  
 Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Ser Met Ser  
 50 55 60  
 Arg Tyr Arg Gly Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr  
 65 70 75 80  
 Lys Arg Phe Ile Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val  
 85 90 95  
 Tyr Glu Glu

<210> 341  
 <211> 431  
 <212> PRT  
 <213> Mouse

<400> 341

Met Asp Ala Arg Trp Trp Ala Val Val Val Leu Ala Thr Leu Pro Ser  
 1 5 10 15  
 Leu Gly Ala Gly Gly Glu Ser Pro Glu Ala Pro Pro Gln Ser Trp Thr  
 20 25 30  
 Gln Leu Trp Leu Phe Arg Phe Leu Leu Asn Val Ala Gly Tyr Ala Ser  
 35 40 45  
 Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Leu Arg Arg Lys Asn  
 50 55 60  
 Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys  
 65 70 75 80  
 Val Phe Gly Asn Glu Pro Lys Ala Pro Asp Glu Val Leu Leu Ala Pro  
 85 90 95  
 Arg Thr Glu Thr Ala Glu Ser Thr Pro Ser Trp Gln Val Leu Lys Leu  
 100 105 110  
 Val Phe Cys Ala Ser Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Ile  
 115 120 125  
 Leu Gln Glu Arg Val Met Thr Gly Ser Tyr Gly Ala Thr Ala Thr Ser  
 130 135 140  
 Pro Gly Glu His Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg  
 145 150 155 160  
 Val Leu Ala Leu Val Val Ala Gly Leu Tyr Cys Val Leu Arg Lys Gln  
 165 170 175  
 Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser  
 180 185 190  
 Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser  
 195 200 205  
 Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met  
 210 215 220  
 Met Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr  
 225 230 235 240  
 Leu Thr Ala Gly Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser  
 245 250 255  
 Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu  
 260 265 270  
 Val Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp  
 275 280 285  
 Gln Asp Ala Leu Phe Ala Tyr Lys Met Ser Ser Val Gln Met Met Phe  
 290 295 300  
 Gly Val Asn Leu Phe Ser Cys Leu Phe Thr Val Gly Ser Leu Leu Glu  
 305 310 315 320  
 Gln Gly Ala Leu Leu Glu Gly Ala Arg Phe Met Gly Arg His Ser Glu  
 325 330 335  
 Phe Ala Leu His Ala Leu Leu Leu Ser Ile Cys Ser Ala Phe Gly Gln  
 340 345 350  
 Leu Phe Ile Phe Tyr Thr Ile Gly Gln Phe Gly Ala Ala Val Phe Thr  
 355 360 365  
 Ile Ile Met Thr Leu Arg Gln Ala Ile Ala Ile Leu Leu Ser Cys Leu  
 370 375 380  
 Leu Tyr Gly His Thr Val Thr Val Val Gly Gly Leu Gly Val Ala Val  
 385 390 395 400  
 Val Phe Thr Ala Leu Leu Leu Arg Val Tyr Ala Arg Gly Arg Lys Gln  
 405 410 415  
 Arg Gly Lys Lys Ala Val Pro Thr Glu Pro Pro Val Gln Lys Val  
 420 425 430

&lt;210&gt; 342

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 342

Leu Lys Phe Ser His Pro Cys Leu Glu Asp His Asn Ser Tyr Cys Ile  
 1 5 10 15  
 Asn Gly Ala Cys Ala Phe His His Glu Leu Lys Gln Ala Ile Cys Arg  
 20 25 30  
 Cys Phe Thr Gly Tyr Thr Gly Gln Arg Cys Glu His Leu Thr Leu Thr  
 35 40 45  
 Ser Tyr Ala  
 50

<210> 343  
 <211> 51  
 <212> PRT  
 <213> Human  
 <400> 343

Leu Lys Phe Ser His Leu Cys Leu Glu Asp His Asn Ser Tyr Cys Ile  
 1 5 10 15  
 Asn Gly Ala Cys Ala Phe His His Glu Leu Glu Lys Ala Ile Cys Arg  
 20 25 30  
 Cys Phe Thr Gly Tyr Thr Gly Glu Arg Cys Glu His Leu Thr Leu Thr  
 35 40 45  
 Ser Tyr Ala  
 50

<210> 344  
 <211> 95  
 <212> PRT  
 <213> Human

<400> 344  
 Ala Ala Ala Leu Leu Leu Leu Leu Ala Leu Tyr Thr Ala Arg Val  
 1 5 10 15  
 Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro Lys Ile Arg Tyr  
 20 25 30  
 Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu  
 35 40 45  
 Glu Lys Met Val Ile Ile Thr Thr Lys Ser Val Ser Arg Tyr Arg Gly  
 50 55 60  
 Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile  
 65 70 75 80  
 Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu  
 85 90 95

<210> 345  
 <211> 77  
 <212> PRT  
 <213> Mouse

<400> 345  
 Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro Lys Ile Arg Tyr Ser Asp  
 1 5 10 15  
 Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu Glu Lys  
 20 25 30  
 Met Val Ile Val Thr Thr Lys Ser Met Ser Arg Tyr Arg Gly Gln Glu  
 35 40 45  
 His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile Lys Trp  
 50 55 60  
 Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu  
 65 70 75

<210> 346  
 <211> 77

<212> PRT  
<213> Human

<400> 346

Ser	Lys	Cys	Lys	Cys	Ser	Arg	Lys	Gly	Pro	Lys	Ile	Arg	Tyr	Ser	Asp
1				5					10					15	
Val	Lys	Lys	Leu	Glu	Met	Lys	Pro	Lys	Tyr	Pro	His	Cys	Glu	Glu	Lys
			20					25					30		
Met	Val	Ile	Ile	Thr	Thr	Lys	Ser	Val	Ser	Arg	Tyr	Arg	Gly	Gln	Glu
		35				40					45				
His	Cys	Leu	His	Pro	Lys	Leu	Gln	Ser	Thr	Lys	Arg	Phe	Ile	Lys	Trp
50						55					60				
Tyr	Asn	Ala	Trp	Asn	Glu	Lys	Arg	Arg	Val	Tyr	Glu	Glu			
65					70					75					

<210> 347  
<211> 215  
<212> PRT  
<213> Mouse

<400> 347

Met	Leu	Ser	Leu	Arg	Ser	Leu	Leu	Pro	His	Leu	Gly	Leu	Phe	Leu	Cys
1				5					10					15	
Leu	Ala	Leu	His	Leu	Ser	Pro	Ser	Leu	Ser	Ala	Ser	Asp	Asn	Gly	Ser
			20					25					30		
Cys	Val	Val	Leu	Asp	Asn	Ile	Tyr	Thr	Ser	Asp	Ile	Leu	Glu	Ile	Ser
		35				40					45				
Thr	Met	Ala	Asn	Val	Ser	Gly	Gly	Asp	Val	Thr	Tyr	Thr	Val	Thr	Val
50						55					60				
Pro	Val	Asn	Asp	Ser	Val	Ser	Ala	Val	Ile	Leu	Lys	Ala	Val	Lys	Glu
65					70					75				80	
Asp	Asp	Ser	Pro	Val	Gly	Thr	Trp	Ser	Gly	Thr	Tyr	Glu	Lys	Cys	Asn
			85					90					95		
Asp	Ser	Ser	Val	Tyr	Tyr	Asn	Leu	Thr	Ser	Gln	Ser	Gln	Ser	Val	Phe
			100					105					110		
Gln	Thr	Asn	Trp	Thr	Val	Pro	Thr	Ser	Glu	Asp	Val	Thr	Lys	Val	Asn
		115				120						125			
Leu	Gln	Val	Leu	Ile	Val	Val	Asn	Arg	Thr	Ala	Ser	Lys	Ser	Ser	Val
		130				135					140				
Lys	Met	Glu	Gln	Val	Gln	Pro	Ser	Ala	Ser	Thr	Pro	Ile	Pro	Glu	Ser
145					150					155				160	
Ser	Glu	Thr	Ser	Gln	Thr	Ile	Asn	Thr	Thr	Pro	Thr	Val	Asn	Thr	Ala
			165					170					175		
Lys	Thr	Thr	Ala	Lys	Asp	Thr	Ala	Asn	Thr	Thr	Ala	Val	Thr	Thr	Ala
			180					185					190		
Asn	Thr	Thr	Ala	Asn	Thr	Thr	Ala	Val	Thr	Thr	Ala	Lys	Thr	Thr	Ala
		195				200						205			
Lys	Ser	Leu	Ala	Ile	Arg	Thr									
210						215									

<210> 348  
<211> 21  
<212> PRT  
<213> Mouse

<400> 348

Gly	Tyr	Ser	Asp	Gly	Tyr	Gln	Val	Cys	Ser	Arg	Phe	Gly	Ser	Lys	Val
1				5					10					15	
Pro	Gln	Phe	Leu	Asn											

<210> 349

<211> 417  
 <212> DNA  
 <213> Mouse

<400> 349  
 gctagccgtg caccagctc tccggagcgc gtgcaggcga gccgagcgcc ccgtccgcgg 60  
 ttctcgggca ggcgtgcgg gctccccggc tccccgccgt cccgggcacc cgggcgggccc 120  
 atgcgcccgg gctagagcgt agccgcgggc atgcgcctcc cgtgctgct cgcgcgctc 180  
 tgcctcgcgg cctccccggc gccgcgcgc gcctgccagc tgcgctcgga gtggagaccc 240  
 ttgagcgaag gctgccgcgc cgagctagcc gagaccatcg tgtatgccaa ggtgctggcg 300  
 ctgcaccccg aggtgcctgg cctctacaac tacctgccgt ggcagtacca agctggagag 360  
 ggagggctct tctactccgc cgaggtggag atgcttgtgt gaccaaggcg tggggca 417

<210> 350  
 <211> 1837  
 <212> DNA  
 <213> Mouse

<400> 350  
 cccccactcg ccagccaaag ccgagtgcgc cgggctttgt tcgctttgtc ctgcgcacc 60  
 taagcggcgg gcttgggaaga acgccatccc ggagagcgca cgcggcgctc caccaggtct 120  
 aacaacatgc ctccacttct gcttctacca gccatctaca tgctcctgtt cttcagagtg 180  
 tccccgacca tctctcttca ggaagtgcac gtgaaccggg agaccatggg gaagatcgct 240  
 gtggccagca aattaatgtg gtgctcagcc gcggctcgaca tcctgtttct gttagatggc 300  
 tctcacagca tcgggaaggg gagcttcgag aggtccaagc gcttcgccat cgctgcctgt 360  
 gatgccctgg acatcagccc tggcagggtc agagtgcgag ccttgcagtt tggttccact 420  
 cctcatctgg aattccccct ggactccttc tcaactcgac aggaagtga ggaaagcatc 480  
 aaggggatag ttttcaaagg tgggcgcacc gagacgggccc tagccctgaa acgcctgagc 540  
 agagggttcc ccggaggcag aaatggctct gtgccccaga ttcttatcat cgtcacggat 600  
 ggcaagtccc agggggccgt ggctctcccg gctaagcagc tgagagaaaag gggcatcgtc 660  
 gtgtttgccg taggagtcgc ttttcccagg tgggacgagc tgctcacgct ggccagttag 720  
 ccgaaggacc ggcattgtgt gttggctgag caagtggagg atgccacca tggcctcctc 780  
 agcacctca gcagctccgc actctgcacc actgctgac cagactgcag ggtggaacct 840  
 catccctgtg agcggaggac gctggagacc gtcaggggagc tcgctggcaa tgccttgtgc 900  
 tggagaggat caaggcaagc agacactgtg ctggtctctgc cctgtccctt ctacagctgg 960  
 aagagagtgt tccagacaca ccctgccaac tgctacagaa ccatctgtcc aggccctgt 1020  
 gactcccagc cctgccaaaa tggaggcacg tgcattccag aaggtgtgga taggtaccac 1080  
 tgtctctgcc cactggcatt cggaggggaa gtcaactgtg ccccgaaagt gagcctggaa 1140  
 tgcagaatcg atgtcctctt cctgctggac agttctgcag gcaccacatt ggggggcttc 1200  
 cggagggccca aggcctttgt caagcgcttt gtgcaggccg tgctgaggga ggactccga 1260  
 gccgcgcttg ggatagccag ttatggcagg aatctaattg tggcggtgcc ctgtcgggga 1320  
 gtaccagcat tgtgccggac ctgatcagga gccttgacag cattcccttc agcgggtggc 1380  
 cgaccctaac cgggagtgcc ttgtccagg tggcagagca cggctttggg agtgccagca 1440  
 ggactggtca ggacaggcca cgcagagtag tagttctgct cactgaatca cgctcccagg 1500  
 atgaggtgtc tggggccagca gctcacgcaa gggtcggga gctactcctc ctgggcgtgg 1560  
 gcagttagat cctgcaggcg gagctggtga agatcaccgg tagcccgaa catgtgatgg 1620  
 tccacacaga cctcaggac ctgtcagcca aatccagagc tgcagaggag gctatgcagc 1680  
 cagccacggc caggctgcca ggcacagtca ctggacctgg tcttctgtg gatgcctctg 1740  
 ctctgtggga cgtgagaact ttgccc aaat gcagagcttc atcaggaaat gcaccctccg 1800  
 gtttgatgtg aatcctgatg tgacacaagt tggcctg 1837

<210> 351  
 <211> 941  
 <212> DNA  
 <213> Mouse

<400> 351  
 taagccctca ggccctccta atgctatccc cctttgttcc tgcagcgtgg acccagtcag 60  
 cagccaggcc atggagctct ctgatgtcac cctcattgag ggtgtgggta acgaggtgat 120  
 ggtggttagca ggcgtggtgg cgtgactct agccctggc ctagcctggc tctccaccta 180  
 tgtagcagac agtggttaaca accagctgct gggcaccatt gtgtcagcag gtgacacgtc 240



tgttctccac	ctgggcatg	tggaccagct	ggtaaaccac	ggcactccag	agccaaccga	300
acacccccat	ccatcagggg	gcaatgatga	caaggctgaa	gagaccagt	acagtggggg	360
agacgccact	ggagaacctg	gagctagggg	agagatggag	cccagcctgg	agcatctcct	420
ggacatccaa	ggcctgccta	aaaggcaagc	aggcctgggg	agcagtcgcc	cagaagcccc	480
gctgggggta	gatgatggct	cctgcctctc	tcccagcccc	agcctcatca	atgttcgcct	540
caagttccctc	aatgacacgg	aggagctagc	tgtggccagg	ccagaggaca	ctgtgggtac	600
cctaaaaagg	tgagtagggc	ggagagaggg	cagttgctcg	tgacttgctc	ctcagatgat	660
ggtttctctga	agaagctgtg	catatatgtg	agcacaggag	ggattttaag	gggaaatgga	720
gacttccata	gacagacctt	cagtgtcttt	catgtccagg	ccttgatctc	tctagcctta	780
ttctttatcc	agtctttcct	ttcatccttg	tagcaaatac	ttccctggac	aagagaacca	840
aatgaagttg	atctaccagg	gtcggctgct	gcaggaccca	gcacgcacac	tgagttccct	900
gaacattacc	aacaactgctg	tgatccactg	ccaccgctca	c		941

&lt;210&gt; 352

&lt;211&gt; 571

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 352

gctgactgta	cctataattc	accatgaatt	acgtctgtga	gttacctccg	tgagctctca	60
ttgtgatgtg	agtatgtgtg	catgtgggtg	gggctcagct	gctgtgcgcc	tgacatccac	120
atttgatgt	cttttggttc	cgtgaacaag	tagaaattgc	atgtgtctac	cggtgacagt	180
gtgggtgcac	tgggcccctgt	gggtggtctc	cttacctctg	attccgtctg	tgggaaagtc	240
ccagtgtacc	caaagtgtggc	attgttgcac	gccttgggtg	tgtgtgggag	attgtctctg	300
tctctcagac	cctttgtggc	tttgtctgtt	gaaagagaca	gagaccctt	gtggttttct	360
cagctgagaa	ccctccctcc	tgggatgttg	ggtgtaaact	taactgcttt	gcaaagcctg	420
ccccctctca	tgctgacctt	tcaatatctg	gcagtgcatt	gttcccaagc	cccccttgct	480
tatggaatg	tcagggtctt	ctcaccttga	cagctgataa	ttccattcct	cgactcttga	540
gaactggccc	ttgctttgtt	ttctctgctt	g			571

&lt;210&gt; 353

&lt;211&gt; 467

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 353

cggagaatga	gcgggtggcc	gtggctgcag	ctgctgcggc	ggcactgaca	ggacacgagc	60
tctatgcctt	tccggctgct	tatcccgtc	ggcctcgtgt	gcgtgctgct	gccccgcac	120
carggtgcgc	caggccccga	aggcaccgag	cccgaccccg	cccactacag	ggagcgagtc	180
aaggccatgt	tctaccacgc	ctacgacagt	tacctggaaa	atgcctttcc	ctacgatgag	240
ctgagacctc	tcacctgtga	cgggcacgac	acctggggca	gtttttctct	gacactgatt	300
gatgccttgg	acaccttgct	gattttgggg	aatacctctg	aattccaaag	agtgggtggag	360
gttctccagg	acaaacgtgg	actttgatat	cgacgtcaat	gcctctgtgt	tcgaaaccaa	420
catccgagtg	gtaggaggac	tcctttctgc	tcattctctt	tcaaaga		467

&lt;210&gt; 354

&lt;211&gt; 528

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 354

gtgactcctg	ctgtaggacc	ctccaggaag	cactggcctc	tcctacagag	tcctccacct	60
agcaccggcc	ttaatgctaa	agccaaatgt	ggttttctg	ctgcagcgtg	cccctggtaa	120
tctcgagttg	ccactcccaa	gccagcccc	actggccata	tggcatcata	tctgggggtc	180
aggaggcct	gtgcaggctt	tggacagcca	cttgccacag	cagaggagag	agtgaggttt	240
ccaggagcag	caggaaggaa	gacccagaa	ttccccagg	ctctttgagt	ggtaatgttg	300
acttctggag	agtctgcccc	ccttgtgctc	acacaagcat	ggacaggaca	ctgggacttt	360
tatcctgttg	ttaagctgtt	tccacagaag	ccggttcagg	tagttaactc	acccacattg	420
gcccataagc	cagaggagtg	ccctggctaa	ctgcagtgtg	agcttgtaag	caacagaagt	480
gcccaggagc	tgaccccaaa	ggccaggaag	gctcgagctt	gccacttt		528

<210> 355  
 <211> 473  
 <212> DNA  
 <213> Mouse

<400> 355  
 ggcagcagga ccgcgggtcac tgagcctctg caggtgtcaa caaggetcaa ggagcaggat 60  
 ggatctcgat gtggttaaca tgtttgtgat tgcgggtggg accctggcca ttccaatcct 120  
 ggcatttgtt gcgtctttcc tcctgtggcc ttacgactg ataagaatct attatttgta 180  
 ctggcggagg acactgggca tgcaagtctg ctacgcacac catgaggact atcagttctg 240  
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 <212> DNA  
 <213> Mouse

<400> 357  
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 <212> DNA

&lt;213&gt; Rat

&lt;400&gt; 358

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&lt;210&gt; 359

&lt;211&gt; 1134

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 359

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&lt;210&gt; 360

&lt;211&gt; 876

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 360

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 <212> DNA  
 <213> Mouse

<400> 361						
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<210> 362  
 <211> 349  
 <212> DNA  
 <213> Mouse

<400> 362						
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accaaggcca	gatgcgagcc	accagagaagt	taattaaacc	aggttcctcg	ggagtttgc	300
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<210> 363  
 <211> 380  
 <212> DNA  
 <213> Mouse

<400> 363						
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<210> 364  
 <211> 351  
 <212> DNA  
 <213> Mouse

<400> 364						
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&lt;210&gt; 365

&lt;211&gt; 854

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 365

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&lt;210&gt; 366

&lt;211&gt; 257

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 366

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caaaccaaca	tcctgaa					257

&lt;210&gt; 367

&lt;211&gt; 475

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 367

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&lt;210&gt; 368

&lt;211&gt; 392

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 368

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&lt;210&gt; 369

&lt;211&gt; 824

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 369

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&lt;210&gt; 370

&lt;211&gt; 1663

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 370

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 <211> 568  
 <212> DNA  
 <213> Human

<400> 371  
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<211> 83  
 <212> PRT  
 <213> Mouse

<400> 373  
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 Ala Pro Ala Arg Ala Cys Gln Leu Pro Ser Glu Trp Arg Pro Leu Ser  
 20 25 30  
 Glu Gly Cys Arg Ala Glu Leu Ala Glu Thr Ile Val Tyr Ala Lys Val  
 35 40 45  
 Leu Ala Leu His Pro Glu Val Pro Gly Leu Tyr Asn Tyr Leu Pro Trp  
 50 55 60  
 Gln Tyr Gln Ala Gly Glu Gly Gly Leu Phe Tyr Ser Ala Glu Val Glu  
 65 70 75 80  
 Met Leu Val

<210> 374  
 <211> 405  
 <212> PRT  
 <213> Mouse

<400> 374  
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 20 25 30  
 Thr Met Gly Lys Ile Ala Val Ala Ser Lys Leu Met Trp Cys Ser Ala  
 35 40 45  
 Ala Val Asp Ile Leu Phe Leu Leu Asp Gly Ser His Ser Ile Gly Lys  
 50 55 60  
 Gly Ser Phe Glu Arg Ser Lys Arg Phe Ala Ile Ala Ala Cys Asp Ala  
 65 70 75 80  
 Leu Asp Ile Ser Pro Gly Arg Val Arg Val Gly Ala Leu Gln Phe Gly  
 85 90 95  
 Ser Thr Pro His Leu Glu Phe Pro Leu Asp Ser Phe Ser Thr Arg Gln  
 100 105 110  
 Glu Val Lys Glu Ser Ile Lys Gly Ile Val Phe Lys Gly Gly Arg Thr  
 115 120 125  
 Glu Thr Gly Leu Ala Leu Lys Arg Leu Ser Arg Gly Phe Pro Gly Gly  
 130 135 140  
 Arg Asn Gly Ser Val Pro Gln Ile Leu Ile Ile Val Thr Asp Gly Lys  
 145 150 155 160  
 Ser Gln Gly Pro Val Ala Leu Pro Ala Lys Gln Leu Arg Glu Arg Gly  
 165 170 175  
 Ile Val Val Phe Ala Val Gly Val Arg Phe Pro Arg Trp Asp Glu Leu  
 180 185 190  
 Leu Thr Leu Ala Ser Glu Pro Lys Asp Arg His Val Leu Leu Ala Glu  
 195 200 205  
 Gln Val Glu Asp Ala Thr Asn Gly Leu Leu Ser Thr Leu Ser Ser Ser  
 210 215 220  
 Ala Leu Cys Thr Thr Ala Asp Pro Asp Cys Arg Val Glu Pro His Pro  
 225 230 235 240  
 Cys Glu Arg Arg Thr Leu Glu Thr Val Arg Glu Leu Ala Gly Asn Ala  
 245 250 255  
 Leu Cys Trp Arg Gly Ser Arg Gln Ala Asp Thr Val Leu Ala Leu Pro  
 260 265 270  
 Cys Pro Phe Tyr Ser Trp Lys Arg Val Phe Gln Thr His Pro Ala Asn  
 275 280 285  
 Cys Tyr Arg Thr Ile Cys Pro Gly Pro Cys Asp Ser Gln Pro Cys Gln

290 295 300  
 Asn Gly Gly Thr Cys Ile Pro Glu Gly Val Asp Arg Tyr His Cys Leu  
 305 310 315 320  
 Cys Pro Leu Ala Phe Gly Gly Glu Val Asn Cys Ala Pro Lys Leu Ser  
 325 330 335  
 Leu Glu Cys Arg Ile Asp Val Leu Phe Leu Leu Asp Ser Ser Ala Gly  
 340 345 350  
 Thr Thr Leu Gly Gly Phe Arg Arg Ala Lys Ala Phe Val Lys Arg Phe  
 355 360 365  
 Val Gln Ala Val Leu Arg Glu Asp Ser Arg Ala Arg Val Gly Ile Ala  
 370 375 380  
 Ser Tyr Gly Arg Asn Leu Met Val Ala Val Pro Cys Arg Gly Val Pro  
 385 390 395 400  
 Ala Leu Cys Arg Thr  
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<210> 375  
 <211> 180  
 <212> PRT  
 <213> Mouse

<400> 375  
 Met Glu Leu Ser Asp Val Thr Leu Ile Glu Gly Val Gly Asn Glu Val  
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 Met Val Val Ala Gly Val Val Ala Leu Thr Leu Ala Leu Val Leu Ala  
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 Trp Leu Ser Thr Tyr Val Ala Asp Ser Gly Asn Asn Gln Leu Leu Gly  
 35 40 45  
 Thr Ile Val Ser Ala Gly Asp Thr Ser Val Leu His Leu Gly His Val  
 50 55 60  
 Asp Gln Leu Val Asn Gln Gly Thr Pro Glu Pro Thr Glu His Pro His  
 65 70 75 80  
 Pro Ser Gly Gly Asn Asp Asp Lys Ala Glu Glu Thr Ser Asp Ser Gly  
 85 90 95  
 Gly Asp Ala Thr Gly Glu Pro Gly Ala Arg Gly Glu Met Glu Pro Ser  
 100 105 110  
 Leu Glu His Leu Leu Asp Ile Gln Gly Leu Pro Lys Arg Gln Ala Gly  
 115 120 125  
 Leu Gly Ser Ser Arg Pro Glu Ala Pro Leu Gly Leu Asp Asp Gly Ser  
 130 135 140  
 Cys Leu Ser Pro Ser Pro Ser Leu Ile Asn Val Arg Leu Lys Phe Leu  
 145 150 155 160  
 Asn Asp Thr Glu Glu Leu Ala Val Ala Arg Pro Glu Asp Thr Val Gly  
 165 170 175  
 Thr Leu Lys Arg  
 180

<210> 376  
 <211> 68  
 <212> PRT  
 <213> Mouse

<400> 376  
 Met Cys Leu Pro Val Thr Val Trp Cys His Trp Ala Leu Trp Val Ala  
 1 5 10 15  
 His Leu Pro Leu Ile Pro Ser Val Gly Lys Ser Gln Cys Thr Gln Met  
 20 25 30  
 Trp His Cys Cys Met Pro Trp Val Cys Val Gly Asp Cys Leu Cys Leu  
 35 40 45  
 Ser Asp Pro Leu Trp Leu Cys Leu Leu Lys Glu Thr Glu Thr Pro Cys  
 50 55 60

Gly Phe Leu Ser  
65

<210> 377  
<211> 107  
<212> PRT  
<213> Rat

<400> 377  
Met Pro Phe Arg Leu Leu Ile Pro Leu Gly Leu Val Cys Val Leu Leu  
1 5 10 15  
Pro Leu His His Gly Ala Pro Gly Pro Glu Gly Thr Ala Pro Asp Pro  
20 25 30  
Ala His Tyr Arg Glu Arg Val Lys Ala Met Phe Tyr His Ala Tyr Asp  
35 40 45  
Ser Tyr Leu Glu Asn Ala Phe Pro Tyr Asp Glu Leu Arg Pro Leu Thr  
50 55 60  
Cys Asp Gly His Asp Thr Trp Gly Ser Phe Ser Leu Thr Leu Ile Asp  
65 70 75 80  
Ala Leu Asp Thr Leu Leu Ile Leu Gly Asn Thr Ser Glu Phe Gln Arg  
85 90 95  
Val Val Glu Val Leu Gln Asp Lys Arg Gly Leu  
100 105

<210> 378  
<211> 95  
<212> PRT  
<213> Rat

<400> 378  
Met Trp Phe Leu Pro Cys Ser Val Pro Leu Val Ile Ser Ser Cys His  
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20 25 30  
Glu Gly Leu Cys Arg Leu Trp Thr Ala Thr Cys His Ser Arg Gly Glu  
35 40 45  
Ser Glu Val Ser Arg Ser Ser Arg Lys Glu Asp Pro Arg Ile Pro Gln  
50 55 60  
Gly Ser Leu Ser Gly Asn Val Asp Phe Trp Arg Val Cys Pro Pro Cys  
65 70 75 80  
Ala His Thr Ser Met Asp Arg Thr Leu Gly Leu Leu Ser Cys Cys  
85 90 95

<210> 379  
<211> 138  
<212> PRT  
<213> Mouse

<400> 379  
Met Asp Leu Asp Val Val Asn Met Phe Val Ile Ala Gly Gly Thr Leu  
1 5 10 15  
Ala Ile Pro Ile Leu Ala Phe Val Ala Ser Phe Leu Leu Trp Pro Ser  
20 25 30  
Ala Leu Ile Arg Ile Tyr Tyr Trp Tyr Trp Arg Arg Thr Leu Gly Met  
35 40 45  
Gln Val Arg Tyr Ala His His Glu Asp Tyr Gln Phe Cys Tyr Ser Phe  
50 55 60  
Arg Gly Arg Pro Gly His Lys Pro Ser Ile Leu Met Leu His Gly Phe  
65 70 75 80  
Ser Ala His Lys Asp Met Trp Leu Ser Val Val Lys Phe Leu Pro Lys  
85 90 95

Asn Leu His Leu Val Cys Val Asp Met Pro Gly His Glu Gly Thr Thr  
 100 105 110  
 Arg Ser Ser Leu Asp Asp Leu Ser Ile Val Gly Gln Val Lys Arg Ile  
 115 120 125  
 His Gln Phe Val Glu Cys Leu Lys Leu Asn  
 130 135

&lt;210&gt; 380

&lt;211&gt; 81

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 380

Met Ala Ser Ser Ser Asn Trp Leu Ser Gly Val Asn Val Val Leu Val  
 1 5 10 15  
 Met Ala Tyr Gly Ser Leu Val Phe Val Leu Leu Phe Ile Phe Val Lys  
 20 25 30  
 Arg Gln Ile Met Arg Phe Ala Met Lys Ser Arg Arg Gly Pro His Val  
 35 40 45  
 Pro Val Gly His Asn Ala Pro Lys Asp Leu Lys Glu Glu Ile Asp Ile  
 50 55 60  
 Arg Leu Ser Arg Val Gln Asp Ile Lys Tyr Glu Pro Gln Leu Leu Ala  
 65 70 75 80  
 Asp

&lt;210&gt; 381

&lt;211&gt; 257

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 381

Met Arg Ser Gly Ala Leu Trp Pro Leu Leu Trp Gly Ala Leu Val Trp  
 1 5 10 15  
 Thr Val Gly Ser Val Gly Ala Val Met Gly Ser Glu Asp Ser Val Pro  
 20 25 30  
 Gly Gly Val Cys Trp Leu Gln Gln Gly Arg Glu Ala Thr Cys Ser Leu  
 35 40 45  
 Val Leu Lys Thr Arg Val Ser Arg Glu Glu Cys Cys Ala Ser Gly Asn  
 50 55 60  
 Ile Asn Thr Ala Trp Ser Asn Phe Thr His Pro Gly Asn Lys Ile Ser  
 65 70 75 80  
 Leu Leu Gly Phe Leu Gly Leu Val His Cys Leu Pro Cys Lys Asp Ser  
 85 90 95  
 Cys Asp Gly Val Glu Cys Gly Pro Gly Lys Ala Cys Arg Met Leu Gly  
 100 105 110  
 Gly Arg Pro Thr Leu Arg Ser Cys Val Pro Asn Cys Glu Gly Leu Pro  
 115 120 125  
 Ala Gly Phe Gln Val Cys Gly Ser Asp Gly Ala Thr Tyr Arg Asp Glu  
 130 135 140  
 Cys Glu Leu Arg Thr Ala Arg Cys Arg Gly His Pro Asp Leu Arg Val  
 145 150 155 160  
 Met Tyr Arg Gly Arg Cys Gln Lys Ser Cys Ala Gln Val Val Cys Pro  
 165 170 175  
 Arg Pro Gln Ser Cys Leu Val Asp Gln Thr Gly Ser Ala His Cys Val  
 180 185 190  
 Val Cys Arg Ala Ala Pro Cys Pro Val Pro Ser Asn Pro Gly Gln Glu  
 195 200 205  
 Leu Cys Gly Asn Asn Asn Val Thr Tyr Ile Ser Ser Cys His Leu Arg  
 210 215 220  
 Gln Ala Thr Cys Phe Leu Gly Arg Ser Ile Gly Val Arg His Pro Gly

<210>	382
<211>	285
<212>	PRT
<213>	Rat

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<210> 383
<211> 183
<212> PRT
<213> Rat
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154

Ser Gln Lys Asp Cys Asn Cys Leu His Val Val Glu Pro Met Pro Val  
 50 55 60  
 Pro Gly His Asp Val Glu Ala Tyr Cys Leu Leu Cys Glu Cys Arg Tyr  
 65 70 75 80  
 Glu Glu Arg Ser Thr Thr Thr Ile Lys Val Ile Ile Val Ile Tyr Leu  
 85 90 95  
 Ser Val Val Gly Ala Leu Leu Leu Tyr Met Ala Phe Leu Met Leu Val  
 100 105 110  
 Asp Pro Leu Ile Arg Lys Pro Asp Ala Tyr Thr Glu Gln Leu His Asn  
 115 120 125  
 Glu Glu Glu Asn Glu Asp Ala Arg Ser Met Ala Ala Ala Ala Ala Ser  
 130 135 140  
 Ile Gly Gly Pro Arg Ala Asn Thr Val Leu Glu Arg Val Glu Gly Ala  
 145 150 155 160  
 Gln Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Thr Val Phe  
 165 170 175  
 Asp Arg His Lys Met Leu Ser  
 180

<210> 384  
 <211> 292  
 <212> PRT  
 <213> Mouse

<400> 384  
 Cys Gln Leu Pro Leu Arg Val Leu Ile Ile Ser Asn Asn Lys Leu Gly  
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 Ala Leu Pro Pro Asp Ile Ser Thr Leu Gly Ser Leu Arg Gln Leu Asp  
 20 25 30  
 Val Ser Ser Asn Glu Leu Gln Ser Leu Pro Val Glu Leu Cys Ser Leu  
 35 40 45  
 Arg Ser Leu Arg Asp Leu Asn Val Arg Arg Asn Gln Leu Ser Thr Leu  
 50 55 60  
 Pro Asp Glu Leu Gly Asp Leu Pro Leu Val Arg Leu Asp Phe Ser Cys  
 65 70 75 80  
 Asn Arg Ile Ser Arg Ile Pro Val Ser Phe Cys Arg Leu Arg His Leu  
 85 90 95  
 Gln Val Val Leu Leu Asp Ser Asn Pro Leu Gln Ser Pro Pro Ala Gln  
 100 105 110  
 Ile Cys Leu Lys Gly Lys Leu His Ile Phe Lys Tyr Leu Thr Met Glu  
 115 120 125  
 Ala Gly Arg Arg Gly Ala Ala Leu Gly Asp Leu Val Pro Ser Arg Pro  
 130 135 140  
 Pro Ser Phe Ser Pro Cys Pro Ala Glu Asp Leu Phe Pro Gly Arg Arg  
 145 150 155 160  
 Tyr Asp Gly Gly Leu Asp Ser Gly Phe His Ser Val Asp Ser Gly Ser  
 165 170 175  
 Lys Arg Trp Ser Gly Asn Glu Ser Thr Asp Asp Phe Ser Glu Leu Ser  
 180 185 190  
 Phe Arg Ile Ser Glu Leu Ala Arg Asp Pro Arg Gly Pro Arg Gln Pro  
 195 200 205  
 Arg Glu Asp Gly Ala Gly Asp Gly Asp Leu Glu Gln Ile Asp Phe Ile  
 210 215 220  
 Asp Ser His Val Pro Gly Glu Asp Glu Asp Arg Ser Ala Ala Glu Glu  
 225 230 235 240  
 Gln Leu Pro Ser Glu Leu Ser Leu Val Ala Gly Asp Val Glu Lys Pro  
 245 250 255  
 Ser Ser Ser Arg Arg Glu Glu Pro Ala Gly Glu Glu Arg Arg Arg Pro  
 260 265 270  
 Asp Thr Leu Gln Leu Trp Gln Glu Arg Glu Arg Lys Gln Gln Gln Gln  
 275 280 285

Ser Gly Gly Trp  
290

<210> 385  
<211> 164  
<212> PRT  
<213> Mouse

<400> 385  
Ser Arg Gln Leu Arg Ala Pro Arg Phe Asp Pro Arg Ala Gly Phe His  
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20 25 30  
Ala Ala Arg Ser Ser Gly Gln Leu Asn Leu Ala Gly Arg Asn Leu Gly  
35 40 45  
Glu Val Pro Gln Cys Val Trp Arg Ile Asn Val Asp Ile Pro Glu Glu  
50 55 60  
Ala Asn Gln Asn Leu Ser Phe Ser Ser Thr Glu Arg Trp Trp Asp Gln  
65 70 75 80  
Thr Asp Leu Thr Lys Leu Ile Ile Ser Ser Asn Lys Leu Gln Ser Leu  
85 90 95  
Ser Asp Asp Leu Arg Leu Leu Pro Ala Leu Thr Val Leu Asp Ile His  
100 105 110  
Asp Asn Gln Leu Thr Ser Leu Pro Ser Ala Ile Arg Glu Leu Asp Asn  
115 120 125  
Leu Gln Lys Leu Asn Val Ser His Asn Lys Leu Lys Ile Leu Pro Glu  
130 135 140  
Glu Ile Thr Ser Leu Lys Asn Leu Arg Thr Leu His Leu Gln His Asn  
145 150 155 160  
Glu Leu Thr Cys

<210> 386  
<211> 71  
<212> PRT  
<213> Mouse

<400> 386  
Ser Leu Ser Ile Leu Pro Ala Val Arg Val Ser Pro Arg Pro Thr Tyr  
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Pro Ser Thr Ala Ser Ser Met Ala Ala Phe Leu Val Thr Gly Phe Phe  
20 25 30  
Phe Ser Leu Phe Val Val Leu Gly Met Glu Pro Arg Ala Leu Phe Arg  
35 40 45  
Pro Asp Lys Ala Leu Pro Leu Ser Cys Ala Lys Pro Thr Ser Leu Cys  
50 55 60  
Val Gln Ser Ser Phe Leu Gly  
65 70

<210> 387  
<211> 126  
<212> PRT  
<213> Mouse

<400> 387  
Glu Tyr Glu Ala Arg Val Leu Glu Lys Ser Leu Arg Lys Glu Ser Arg  
1 5 10 15  
Asn Lys Glu Thr Asp Lys Val Lys Leu Thr Trp Arg Asp Arg Phe Pro  
20 25 30  
Ala Tyr Phe Thr Asn Leu Val Ser Ile Ile Phe Met Ile Ala Val Thr  
35 40 45

Phe Ala Ile Val Leu Gly Val Ile Ile Tyr Arg Ile Ser Thr Ala Ala  
 50 55 60  
 Ala Leu Ala Met Asn Ser Ser Pro Ser Val Arg Ser Asn Ile Arg Val  
 65 70 75 80  
 Thr Val Thr Ala Thr Ala Val Ile Ile Asn Leu Val Val Ile Ile Leu  
 85 90 95  
 Leu Asp Glu Val Tyr Gly Cys Ile Ala Arg Trp Leu Thr Lys Ile Gly  
 100 105 110  
 Glu Cys His Val Gln Asp Ser Ile Gly Ser Met Gly Leu Gly  
 115 120 125

&lt;210&gt; 388

&lt;211&gt; 84

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 388

Ala Ala Glu Asn Glu Met Pro Val Ala Val Gly Pro Tyr Gly Gln Ser  
 1 5 10 15  
 Gln Pro Ser Cys Phe Asp Arg Val Lys Met Gly Phe Val Met Gly Cys  
 20 25 30  
 Ala Val Gly Met Ala Ala Gly Ala Leu Phe Gly Thr Phe Ser Cys Leu  
 35 40 45  
 Arg Ile Gly Met Arg Gly Arg Glu Leu Met Gly Gly Ile Gly Lys Thr  
 50 55 60  
 Met Met Gln Ser Gly Gly Thr Phe Gly Thr Phe Met Ala Ile Gly Met  
 65 70 75 80  
 Gly Ile Arg Cys

&lt;210&gt; 389

&lt;211&gt; 284

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 389

Gly Gly Ser Ser Val Ser His Val Leu Arg Gly Ser Gly Gln Glu Arg  
 1 5 10 15  
 Ser Pro Pro Pro Ala Ser Met Gln Pro Pro Trp Gly Leu Ala Leu Pro  
 20 25 30  
 Leu Leu Leu Pro Trp Val Ala Gly Gly Val Gly Thr Ser Pro Arg Asp  
 35 40 45  
 Tyr Trp Leu Pro Ala Leu Ala His Gln Pro Gly Val Cys His Tyr Gly  
 50 55 60  
 Thr Lys Thr Ala Cys Cys Tyr Gly Trp Lys Arg Asn Ser Lys Gly Val  
 65 70 75 80  
 Cys Glu Ala Val Cys Glu Pro Arg Cys Lys Phe Gly Glu Cys Val Gly  
 85 90 95  
 Pro Asn Lys Cys Arg Cys Phe Pro Gly Tyr Thr Gly Lys Thr Cys Ser  
 100 105 110  
 Gln Asp Val Asn Glu Cys Ala Phe Lys Pro Arg Pro Cys Gln His Arg  
 115 120 125  
 Cys Val Asn Thr His Gly Ser Tyr Lys Cys Phe Cys Leu Ser Gly His  
 130 135 140  
 Met Leu Leu Pro Asp Ala Thr Cys Ser Asn Ser Arg Thr Cys Ala Arg  
 145 150 155 160  
 Ile Asn Cys Gln Tyr Ser Cys Glu Asp Thr Ala Glu Gly Pro Arg Cys  
 165 170 175  
 Val Cys Pro Ser Ser Gly Leu Arg Leu Gly Pro Asn Gly Arg Val Cys  
 180 185 190  
 Leu Asp Ile Asp Glu Cys Ala Ser Ser Lys Ala Val Cys Pro Ser Asn



```
<210> 390
<211> 85
<212> PRT
<213> Rat
```

```
<210> 391
<211> 158
<212> PRT
<213> Rat
```

```
<210> 392
<211> 124
<212> PRT
```

## &lt;213&gt; Mouse

&lt;400&gt; 392

Ala Ala Glu Gln Glu Ala Ser Ser Arg Arg Arg Arg Gly Gly Ala Gly  
 1 5 10 15  
 Pro Ala Leu Phe Ser Ser Gly Ser Leu Arg Ser Glu Pro Gln Pro Arg  
 20 25 30  
 Leu Pro Gln Ala Arg Ser Arg Pro Arg Pro Ser Phe Leu Gln Ala Arg  
 35 40 45  
 Ser Arg Pro Cys Leu Ser Gln Ala Cys Ser Pro Ala Ala Ser Val Leu  
 50 55 60  
 Ser Ser Ser Ser Leu Cys Gly Arg Ser His Leu Leu Pro Gly Ser Leu  
 65 70 75 80  
 Pro Ala Thr Ala Phe Leu Leu Leu Leu Pro Gly Ser Leu Pro Gly Arg  
 85 90 95  
 Arg Pro Ser Ala Ala Gln Ala Ala Pro Val Leu Ala Trp Gly Leu Val  
 100 105 110  
 Ala Phe Gln Leu Gly Val Ala Ala Gly Ala Gly Arg  
 115 120

&lt;210&gt; 393

&lt;211&gt; 242

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 393

Gly His Cys Asp Cys Gln Ala Gly Tyr Gly Gly Glu Ala Cys Gly Gln  
 1 5 10 15  
 Cys Gly Leu Gly Tyr Phe Glu Ala Glu Arg Asn Ser Ser His Leu Val  
 20 25 30  
 Cys Ser Ala Cys Phe Gly Pro Cys Ala Arg Cys Thr Gly Pro Glu Glu  
 35 40 45  
 Ser His Cys Leu Gln Cys Arg Lys Gly Trp Ala Leu His His Leu Lys  
 50 55 60  
 Cys Val Asp Ile Asp Glu Cys Gly Thr Glu Gln Ala Thr Cys Gly Ala  
 65 70 75 80  
 Asp Gln Phe Cys Val Asn Thr Glu Gly Ser Tyr Glu Cys Arg Asp Cys  
 85 90 95  
 Ala Lys Ala Cys Leu Gly Cys Met Gly Ala Gly Pro Gly Pro Cys Lys  
 100 105 110  
 Lys Cys Ser Arg Gly Tyr Gln Gln Val Gly Ser Lys Cys Leu Asp Val  
 115 120 125  
 Asp Glu Cys Glu Thr Val Val Cys Pro Gly Glu Asn Glu Gln Cys Glu  
 130 135 140  
 Asn Thr Glu Gly Ser Tyr Arg Cys Val Cys Ala Glu Gly Phe Arg Gln  
 145 150 155 160  
 Glu Asp Gly Ile Cys Val Lys Glu Gln Ile Pro Glu Ser Ala Gly Phe  
 165 170 175  
 Phe Ala Glu Met Thr Glu Asp Glu Met Val Val Leu Gln Gln Met Phe  
 180 185 190  
 Phe Gly Val Ile Ile Cys Ala Leu Ala Thr Leu Ala Ala Lys Gly Asp  
 195 200 205  
 Leu Val Phe Thr Ala Ile Phe Ile Gly Ala Val Ala Ala Met Thr Gly  
 210 215 220  
 Tyr Trp Leu Ser Glu Arg Ser Asp Arg Val Leu Glu Gly Phe Ile Lys  
 225 230 235 240  
 Gly Arg

&lt;210&gt; 394

&lt;211&gt; 99

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 394

```

Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Ala Leu Cys
 1              5              10              15
Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro
      20              25              30
Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr
      35              40              45
Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Ser Met Ser
      50              55              60
Arg Tyr Arg Gly Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr
65              70              75              80
Lys Arg Phe Ile Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val
      85              90              95
Tyr Glu Glu

```

&lt;210&gt; 395

&lt;211&gt; 103

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 395

```

Met Ala Leu Gly Val Pro Ile Ser Val Tyr Leu Leu Phe Asn Ala Met
 1              5              10              15
Thr Ala Leu Thr Glu Glu Ala Ala Val Thr Val Thr Pro Pro Ile Thr
      20              25              30
Ala Gln Gln Gly Asn Trp Thr Val Asn Lys Thr Glu Ala Asp Asn Ile
      35              40              45
Glu Gly Pro Ile Ala Leu Lys Phe Ser His Leu Cys Leu Glu Asp His
      50              55              60
Asn Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Glu
65              70              75              80
Lys Ala Ile Cys Arg Cys Leu Lys Leu Lys Ser Pro Tyr Asn Val Cys
      85              90              95
Ser Gly Glu Arg Arg Pro Leu
      100

```

&lt;210&gt; 396

&lt;211&gt; 1529

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 396

```

Met Ser Gly Ile Gly Trp Gln Thr Leu Ser Leu Ser Leu Ala Leu Val
 1              5              10              15
Leu Ser Ile Leu Asn Lys Val Ala Pro His Ala Cys Pro Ala Gln Cys
      20              25              30
Ser Cys Ser Gly Ser Thr Val Asp Cys His Gly Leu Ala Leu Arg Ser
      35              40              45
Val Pro Arg Asn Ile Pro Arg Asn Thr Glu Arg Leu Asp Leu Asn Gly
      50              55              60
Asn Asn Ile Thr Arg Ile Thr Lys Thr Asp Phe Ala Gly Leu Arg His
65              70              75              80
Leu Arg Val Leu Gln Leu Met Glu Asn Lys Ile Ser Thr Ile Glu Arg
      85              90              95
Gly Ala Phe Gln Asp Leu Lys Glu Leu Glu Arg Leu Arg Leu Asn Arg
      100              105              110
Asn Asn Leu Gln Leu Phe Pro Glu Leu Leu Phe Leu Gly Thr Ala Lys

```

115	120	125
Leu Tyr Arg Leu Asp	Leu Ser Glu Asn Gln Ile	Gln Ala Ile Pro Arg
130	135	140
Lys Ala Phe Arg Gly	Ala Val Asp Ile Lys	Asn Leu Gln Leu Asp Tyr
145	150	155
Asn Gln Ile Ser Cys	Ile Glu Asp Gly Ala Phe	Arg Ala Leu Arg Asp
165	170	175
Leu Glu Val Leu Thr	Leu Asn Asn Asn Ile Thr	Arg Leu Ser Val
180	185	190
Ala Ser Phe Asn His Met	Pro Lys Leu Arg Thr Phe	Arg Leu His Ser
195	200	205
Asn Asn Leu Tyr Cys	Asp Cys His Leu Ala Trp	Leu Ser Asp Trp Leu
210	215	220
Arg Gln Arg Pro Arg	Val Gly Leu Tyr Thr	Gln Cys Met Gly Pro Ser
225	230	235
His Leu Arg Gly His	Asn Val Ala Glu Val	Gln Lys Arg Glu Phe Val
245	250	255
Cys Ser Gly His Gln	Ser Phe Met Ala Pro	Ser Cys Ser Val Leu His
260	265	270
Cys Pro Ile Ala Cys	Thr Cys Ser Asn Asn	Ile Val Asp Cys Arg Gly
275	280	285
Lys Gly Leu Thr Glu	Ile Pro Thr Asn Leu	Pro Glu Thr Ile Thr Glu
290	295	300
Ile Arg Leu Glu Gln	Asn Ser Ile Arg Val	Ile Pro Pro Gly Ala Phe
305	310	315
Ser Pro Tyr Lys Lys	Leu Arg Arg Leu Asp	Leu Ser Asn Asn Gln Ile
325	330	335
Ser Glu Leu Ala Pro	Asp Ala Phe Gln Gly	Leu Arg Ser Leu Asn Ser
340	345	350
Leu Val Leu Tyr Gly	Asn Lys Ile Thr Glu	Leu Pro Lys Ser Leu Phe
355	360	365
Glu Gly Leu Phe Ser	Leu Gln Leu Leu Leu	Asn Ala Asn Lys Ile
370	375	380
Asn Cys Leu Arg Val	Asp Ala Phe Gln Asp	Leu His Asn Leu Asn Leu
385	390	395
Leu Ser Leu Tyr Asp	Asn Lys Leu Gln Thr	Val Ala Lys Gly Thr Phe
405	410	415
Ser Ala Leu Arg Ala	Ile Gln Thr Met His	Leu Ala Gln Asn Pro Phe
420	425	430
Ile Cys Asp Cys His	Leu Lys Trp Leu Ala	Asp Tyr Leu His Thr Asn
435	440	445
Pro Ile Glu Thr Ser	Gly Ala Arg Cys Thr	Ser Pro Arg Arg Leu Ala
450	455	460
Asn Lys Arg Ile Gly	Gln Ile Lys Ser Lys	Lys Phe Arg Cys Ser Ala
465	470	475
Lys Glu Gln Tyr Phe	Ile Pro Gly Thr Glu	Asp Tyr Arg Ser Lys Leu
485	490	495
Ser Gly Asp Cys Phe	Ala Asp Leu Ala Cys	Pro Glu Lys Cys Arg Cys
500	505	510
Glu Gly Thr Thr Val	Asp Cys Ser Asn Gln	Lys Leu Asn Lys Ile Pro
515	520	525
Asp His Ile Pro Gln	Tyr Thr Ala Glu Leu	Arg Leu Asn Asn Asn Glu
530	535	540
Phe Thr Val Leu Glu	Ala Thr Gly Ile Phe	Lys Lys Leu Pro Gln Leu
545	550	555
Arg Lys Ile Asn Leu	Ser Asn Asn Lys Ile	Thr Asp Ile Glu Glu Gly
565	570	575
Ala Phe Glu Gly Ala	Ser Gly Val Asn Glu	Ile Leu Leu Thr Ser Asn
580	585	590
Arg Leu Glu Asn Val	Gln His Lys Met Phe	Lys Gly Leu Glu Ser Leu
595	600	605

Lys Thr Leu Met Leu Arg Ser Asn Arg Ile Ser Cys Val Gly Asn Asp  
 610 615 620  
 Ser Phe Thr Gly Leu Gly Ser Val Arg Leu Leu Ser Leu Tyr Asp Asn  
 625 630 635 640  
 Gln Ile Thr Thr Val Ala Pro Gly Ala Phe Gly Thr Leu His Ser Leu  
 645 650 655  
 Ser Thr Leu Asn Leu Leu Ala Asn Pro Phe Asn Cys Asn Cys His Leu  
 660 665 670  
 Ala Trp Leu Gly Glu Trp Leu Arg Arg Lys Arg Ile Val Thr Gly Asn  
 675 680 685  
 Pro Arg Cys Gln Lys Pro Tyr Phe Leu Lys Glu Ile Pro Ile Gln Asp  
 690 695 700  
 Val Ala Ile Gln Asp Phe Thr Cys Asp Asp Gly Asn Asp Asp Asn Ser  
 705 710 715 720  
 Cys Ser Pro Leu Ser Arg Cys Pro Ser Glu Cys Thr Cys Leu Asp Thr  
 725 730 735  
 Val Val Arg Cys Ser Asn Lys Gly Leu Lys Val Leu Pro Lys Gly Ile  
 740 745 750  
 Pro Arg Asp Val Thr Glu Leu Tyr Leu Asp Gly Asn Gln Phe Thr Leu  
 755 760 765  
 Val Pro Lys Glu Leu Ser Asn Tyr Lys His Leu Thr Leu Ile Asp Leu  
 770 775 780  
 Ser Asn Asn Arg Ile Ser Thr Leu Ser Asn Gln Ser Phe Ser Asn Met  
 785 790 795 800  
 Thr Gln Leu Leu Thr Leu Ile Leu Ser Tyr Asn Arg Leu Arg Cys Ile  
 805 810 815  
 Pro Pro Arg Thr Phe Asp Gly Leu Lys Ser Leu Arg Leu Leu Ser Leu  
 820 825 830  
 His Gly Asn Asp Ile Ser Val Val Pro Glu Gly Ala Phe Gly Asp Leu  
 835 840 845  
 Ser Ala Leu Ser His Leu Ala Ile Gly Ala Asn Pro Leu Tyr Cys Asp  
 850 855 860  
 Cys Asn Met Gln Trp Leu Ser Asp Trp Val Lys Ser Glu Tyr Lys Glu  
 865 870 875 880  
 Pro Gly Ile Ala Arg Cys Ala Gly Pro Gly Glu Met Ala Asp Lys Leu  
 885 890 895  
 Leu Leu Thr Thr Pro Ser Lys Lys Phe Thr Cys Gln Gly Pro Val Asp  
 900 905 910  
 Val Thr Ile Gln Ala Lys Cys Asn Pro Cys Leu Ser Asn Pro Cys Lys  
 915 920 925  
 Asn Asp Gly Thr Cys Asn Asn Asp Pro Val Asp Phe Tyr Arg Cys Thr  
 930 935 940  
 Cys Pro Tyr Gly Phe Lys Gly Gln Asp Cys Asp Val Pro Ile His Ala  
 945 950 955 960  
 Cys Ile Ser Asn Pro Cys Lys His Gly Gly Thr Cys His Leu Lys Glu  
 965 970 975  
 Gly Glu Asn Asp Gly Phe Trp Cys Thr Cys Ala Asp Gly Phe Glu Gly  
 980 985 990  
 Glu Ser Cys Asp Ile Asn Ile Asp Asp Cys Glu Asp Asn Asp Cys Glu  
 995 1000 1005  
 Asn Asn Ser Thr Cys Val Asp Gly Ile Asn Asn Tyr Thr Cys Leu Cys  
 1010 1015 1020  
 Pro Pro Glu Tyr Thr Gly Glu Leu Cys Glu Glu Lys Leu Asp Phe Cys  
 1025 1030 1035 104  
 Ala Gln Asp Leu Asn Pro Cys Gln His Asp Ser Lys Cys Ile Leu Thr  
 1045 1050 1055  
 Pro Lys Gly Phe Lys Cys Asp Cys Thr Pro Gly Tyr Ile Gly Glu His  
 1060 1065 1070  
 Cys Asp Ile Asp Phe Asp Asp Cys Gln Asp Asn Lys Cys Lys Asn Gly  
 1075 1080 1085  
 Ala His Cys Thr Asp Ala Val Asn Gly Tyr Thr Cys Val Cys Pro Glu

1090	1095	1100
Gly Tyr Ser Gly Leu Phe Cys Glu Phe Ser Pro Pro Met Val Leu Leu		
1105	1110	1115
Arg Thr Ser Pro Cys Asp Asn Phe Asp Cys Gln Asn Gly Ala Gln Cys		
	1125	1130
Ile Ile Arg Val Asn Glu Pro Ile Cys Gln Cys Leu Pro Gly Tyr Leu		
	1140	1145
Gly Glu Lys Cys Glu Lys Leu Val Ser Val Asn Phe Val Asn Lys Glu		
	1155	1160
Ser Tyr Leu Gln Ile Pro Ser Ala Lys Val Arg Pro Gln Thr Asn Ile		
	1170	1175
Thr Leu Gln Ile Ala Thr Asp Glu Asp Ser Gly Ile Leu Leu Tyr Lys		
1185	1190	1195
Gly Asp Lys Asp His Ile Ala Val Glu Leu Tyr Arg Gly Arg Val Arg		
	1205	1210
Ala Ser Tyr Asp Thr Gly Ser His Pro Ala Ser Ala Ile Tyr Ser Val		
	1220	1225
Glu Thr Ile Asn Asp Gly Asn Phe His Ile Val Glu Leu Leu Thr Leu		
	1235	1240
Asp Ser Ser Leu Ser Leu Ser Val Asp Gly Gly Ser Pro Lys Ile Ile		
	1250	1255
Thr Asn Leu Ser Lys Gln Ser Thr Leu Asn Phe Asp Ser Pro Leu Tyr		
1265	1270	1275
Val Gly Gly Met Pro Gly Lys Asn Asn Val Ala Ser Leu Arg Gln Ala		
	1285	1290
Pro Gly Gln Asn Gly Thr Ser Phe His Gly Cys Ile Arg Asn Leu Tyr		
	1300	1305
Ile Asn Ser Glu Leu Gln Asp Phe Arg Lys Val Pro Met Gln Thr Gly		
	1315	1320
Ile Leu Pro Gly Cys Glu Pro Cys His Lys Lys Val Cys Ala His Gly		
	1330	1335
Thr Cys Gln Pro Ser Ser Gln Ser Gly Phe Thr Cys Glu Cys Glu Glu		
1345	1350	1355
Gly Trp Met Gly Pro Leu Cys Asp Gln Arg Thr Asn Asp Pro Cys Leu		
	1365	1370
Gly Asn Lys Cys Val His Gly Thr Cys Leu Pro Ile Asn Ala Phe Ser		
	1380	1385
Tyr Ser Cys Lys Cys Leu Glu Gly His Gly Gly Val Leu Cys Asp Glu		
	1395	1400
Glu Glu Asp Leu Phe Asn Pro Cys Gln Val Ile Lys Cys Lys His Gly		
	1410	1415
Lys Cys Arg Leu Ser Gly Leu Gly Gln Pro Tyr Cys Glu Cys Ser Ser		
1425	1430	1435
Gly Phe Thr Gly Asp Ser Cys Asp Arg Glu Ile Ser Cys Arg Gly Glu		
	1445	1450
Arg Ile Arg Asp Tyr Tyr Gln Lys Gln Gln Gly Tyr Ala Ala Cys Gln		
	1460	1465
Thr Thr Lys Lys Val Ser Arg Leu Glu Cys Arg Gly Gly Cys Ala Gly		
	1475	1480
Gly Gln Cys Cys Gly Pro Leu Arg Ser Lys Arg Arg Lys Tyr Ser Phe		
	1490	1495
Glu Cys Thr Asp Gly Ser Ser Phe Val Asp Glu Val Glu Lys Val Val		
1505	1510	1515
Lys Cys Gly Cys Thr Arg Cys Ala Ser		
	1525	

&lt;210&gt; 397

&lt;211&gt; 8

&lt;212&gt; PRT

&lt;213&gt; Mouse

<400> 397  
Trp Tyr Asn Ala Trp Asn Glu Lys  
1 5

<210> 398  
<211> 7  
<212> PRT  
<213> Mouse

<400> 398  
Met Val Ile Ile Thr Thr Lys  
1 5

<210> 399  
<211> 2206  
<212> DNA  
<213> Rat

<400> 399  
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tggaacatct cagccacac agactaagcg gagactgatg ttggtggcgt tcctcggagc 120  
atccqcggtg actgcaagta ccggtctcct gtggaagaag gctcacgcag aatctccacc 180  
gagcgtcaac agcaagaaga ctgacgctgg agataagggg aagagcaagg acaccggga 240  
agtgtcagc catgaaggaa gcgctgcaga cactgcgcc gagcettacc cagaggagaa 300  
gaagaagaag cggtctggat tcagagacag aaaagtaatg gagtatgaga ataggatccg 360  
agcctactcc acaccagaca aaatcttccg gtattttgccc accttgaaag taatcaacga 420  
acctggtgaa actgaagtgt tcatgacccc acaggacttt gtgcgctcca taacacccaa 480  
tgagaagcag ccagaacact tgggcctgga tcagtacata ataaagcgct tcgatggaaa 540  
gaaaattgcc caggaaacgag aaaagtttgc tgacgaaggc agcatcttct atacccttgg 600  
agagtgtgga ctcatctcct tctctgacta catcttctc acaacggtgc tctccactcc 660  
tcagagaaat ttcgaaattg ccttcaagat gtttgacttg aatggagatg gagaagtaga 720  
catggaggag tttgagcagg ttcaaagcat cattcgctcc cagaccagca tgggcatgcy 780  
tcacagagat cgtccaacta ctgggaacac cctcaagtct ggcttatgtt cggccctcac 840  
gacctacttt ttggagctg atctcaaagg gaaactgacc attaaaaact tcctggaatt 900  
tcagcgtaaa ctgcagcatg acgttctaaa gctggagttt gaacgccatg acccggtaga 960  
cgggagaatc tctgagaggc agttcggtgg catgctgctg gcctacagtg gagtgcagtc 1020  
caagaagctg accgccatgc agaggcagct gaagaagcac ttcaaggatg ggaagggcct 1080  
gactttccag gaggtggaga acttcttcac tttcctgaag aacattaatg acgtggacac 1140  
tgcggttaagc ttttaccaca tggctggagc atccctcgat aaagtgaacca tgcagcaagt 1200  
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ctttgactgc gacggcaatg gggagctgag caataaggag tttgtctcca tcatgaagca 1320  
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catgtggaaa tgtgcccag aaaccgcctg ggactttgct ctacccaaat agtaccacac 1440  
ctcctgcacc ttagcacccc gcaatcctgg agtggccttc atgctgctga tgcttctggg 1500  
agtagtgccc acatcccat ctttctggaa gtgacctctg gcctcagctg gctgacctct 1560  
ccatctccc ctgaccagct cagtgttccg ctaggctctg aatctgcagt cagatcaaag 1620  
gtctaagaca ggaacaagtc ttcaaagcag agaccatagc tcccttaacc agtgcccgt 1680  
gggtaaatgc ggggagccct cccacactgg cagccccagg aggcattctc gcagtctctc 1740  
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aagtttgaa atactctggc aggcaaaggg aagtctgtga tgaacggtaa tgcagatgac 1860  
cctggtaccc tgatctggca gggcacctgg tcaggggaag ggtctgcgtc agacaccagc 1920  
ggcaccagga aggtcttttg ccaccagcac agctcccgat tcaaagtcgc tgctttgagc 1980  
ggctctccag aacctcctgc tctttttttt ttcctcccg gtccctgcga tgccctctct 2040  
gggactctgc ttactagag ccagggtgta gcccctgttc cttgtgtctt gtccctctct 2100  
tatagacctg cagagcgag ctgagagcct atctgcctc tgtctaatac actcgtaaat 2160  
atcactttaa ttatagcact ttgcaggaaa taccctaaaa aaaaaa 2206

<210> 400  
<211> 160  
<212> DNA  
<213> Mouse

<400> 400  
 tcgcaggacg ctccactggac agcttgggct tttttcagtt gattttatgg tttgcatctt 60  
 tctctttctc tttttctggt tcttgttccc ctttccccct ttcctgggtga gaaagcacat 120  
 attactgagc cattgcaagc aatgggaggg gtccacaatg 160

<210> 401

<211> 430

<212> DNA

<213> Rat

<400> 401  
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 tccatggcgt cgctcctgtg ctgtgggcct aagctggccg cctgtggcat cgctccagc 120  
 gcctggggag tgatcatgtt gataatgtc gggatatttt tcaatgtcca ttctgctgtg 180  
 ttaattgagg atgtccctt cacagagaaa gattttgaga acggccctca gaacatatac 240  
 aacctgtacg agcaagtacg ctacaactgt ttcacgcgcg cgggcctcta cctcctcctc 300  
 gggggcttct ccttctgcca agttcgtctc aataagcgca aggaatacat ggtgcgctag 360  
 agcgcagtcg gactctcccc attccccctc ttatttaaag actcctcagt ccactctgtc 420  
 cactcatctg 430

<210> 402

<211> 190

<212> DNA

<213> Rat

<400> 402  
 ccgaatacgc ggccgcgtcg acatactgcc tgtagagtta gtatttctgt tttttatatg 60  
 ttgcacactg aattgaagaa atgttggttt ttcttggttt gttttagttt gtttctttgg 120  
 ttttggtttt ggttttgctt tttacttccc aggtttgact atttgccaat gccgtcgacg 180  
 cgccgcgcaa 190

<210> 403

<211> 1774

<212> DNA

<213> Mouse

<400> 403  
 ccaaagtggg gggcgagggc cggggccggg gggctctggg gctgctgccc accttcgacg 60  
 ccggcgaatt cgcaggctgg gagaaggtgg gctcggggcg cttcgggcag gtgtacaagg 120  
 tgcgccatgt gcactggaag acgtggctcg cgatcaagtg ctgcgccagt ctgcacgtcg 180  
 acgacagggg acgaatggag ctcttgaggg aagctaagaa gatggagatg gccaaagtcc 240  
 gatacattct acctgtgtac ggcataatgcc aggaacctgt cggcttggtc atggagtaca 300  
 tggagacagg ctccctggag aagctgctgg cctcagagcc attgccttg gacctgcgt 360  
 ttgcgcatcg gcacgagaca gccgtgggca tgaacttct gcattgcatg tctccgccac 420  
 tgctgcacct agacctgaag ccagcgaaca tctgtctgga tgcccactac catgtcaaga 480  
 tttctgactt tgggtggccc aagtgcaatg gcatgtccca ctctcatgac ctacagcatg 540  
 atggcctgtt tgggtacaatc gcttacctcc ctccagagcg aattcgtgag aagagccgct 600  
 tgtttgacac caaacatgat gtatacagct tcgccattgt gatctggggg gtgcttacac 660  
 agaagaagcc atttgcatg gaaaagaaca tcctacacat catgatgaaa gtggtaaagg 720  
 gccaccgccc agagctgcca cccatctgca gaccccgccc gcgtgcctgt gccagcctga 780  
 tagggataat gcaacggtgc tggcatgcag acccacaggt gcggcccacc ttccaagaaa 840  
 ttacctctga aacagaagac ctttgtgaga agcctgatga ggaggtgaaa gacctggctc 900  
 atgagccagg cgagaaaagc tctctagagt ccaagagtga ggccaggccc gagtcctcac 960  
 gcctcaagcg cgctctgct ccccccttcg ataacgactg cagtctctcc gagttgctgt 1020  
 cacagtggga ctctgggac tcccagactc ttgaaggccc cgaagagctc agccgaagtt 1080  
 cctctgaatg caagctccca ctgtccagca tgggcaagag gctctcgggg gtgtcctcag 1140  
 tggactcagc cttttcctcc agaggatcgc gtgctactgtc ttttgagcgg gaagcttcaa 1200  
 caggcgacct gggcccccac gacatccaga agaagaagct agtggatgcc atcatatcag 1260  
 gggacaccag caggctgatg aagatcctac agccccaaga tgtggacttg gttctagaca 1320  
 gcagtgccag cctgctgcac ctggctgtgg aggccggaca ggaggagtgt gtcaagtggc 1380



tgctgcttaa	caatgccaac	cccaacctga	ccaacaggaa	gggctctaca	ccactgcata	1440
tggtgtgga	gcggaaggga	cgtggaattg	tggagctact	gctagcccgg	aagaccagtg	1500
tcaatgccaa	ggatgaagac	cagtggactg	ccctgcactt	tgcagcccag	aatggggatg	1560
aggccagcac	aaggctgctg	ctagagaaga	atgcttctgt	caatgagggtg	gactttgagg	1620
gccgaacacc	catgcatgta	gcctgccagc	atggacagga	gaacattgtg	cgcaccctgc	1680
tccgccgtgg	tgtggatgtg	ggcctgcagg	gaaaggatgc	ctgggtgcct	ctgcactatg	1740
ctgcctggca	aggccacctt	cccattggta	agct			1774

&lt;210&gt; 404

&lt;211&gt; 372

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 404

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gactgcccgc	ctctggggct	tccttttagag	gagacagtct	ttacctatct	agactcctgc	120
caccctgact	gctgacttac	agctatgagg	tcccggcttc	tgctgcccgt	gccccatttg	180
ccaacgattc	gggaaatgtc	agaagagctg	tcacatgggg	cagctgggca	ggaacccccca	240
gcgtccccca	gcctggatga	ctacgtcagg	tgtatctgtc	agctggcaca	gcccacctca	300
gtgctggaca	aggtcacagc	ccagagccgt	cccaacagac	cctcccggcc	agcctggact	360
cgagagaaga	gg					372

&lt;210&gt; 405

&lt;211&gt; 396

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 405

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gcctcttcat	tttgttttct	tctccaggct	gaagacctga	acgtcaagtt	ggaaggggag	120
ccttccatgc	ggaaacaaaa	gcagcggccg	cgcccgaggc	ccctcatcat	ccccaccaag	180
gcgggcactt	tcctgccttc	tctgtctac	tccaacatca	ccccttacca	gagccacctg	240
cgctctcccg	tgccgcttgc	tgaccacccc	tctgagcgga	gctttgagcc	ccccctttac	300
acaccacccc	ccattctcag	ccccgtccgg	gaaggctctg	gcctctactt	caatgccatc	360
atatcaacca	gcaacatccc	ggccccctct	gtatca			396

&lt;210&gt; 406

&lt;211&gt; 444

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 406

Met	Leu	Val	Ala	Phe	Leu	Gly	Ala	Ser	Ala	Val	Thr	Ala	Ser	Thr	Gly
1				5				10						15	
Leu	Leu	Trp	Lys	Lys	Ala	His	Ala	Glu	Ser	Pro	Pro	Ser	Val	Asn	Ser
			20					25					30		
Lys	Lys	Thr	Asp	Ala	Gly	Asp	Lys	Gly	Lys	Ser	Lys	Asp	Thr	Arg	Glu
			35				40					45			
Val	Ser	Ser	His	Glu	Gly	Ser	Ala	Ala	Asp	Thr	Ala	Ala	Glu	Pro	Tyr
			50			55				60					
Pro	Glu	Glu	Lys	Lys	Lys	Lys	Arg	Ser	Gly	Phe	Arg	Asp	Arg	Lys	Val
65					70				75					80	
Met	Glu	Tyr	Glu	Asn	Arg	Ile	Arg	Ala	Tyr	Ser	Thr	Pro	Asp	Lys	Ile
			85					90					95		
Phe	Arg	Tyr	Phe	Ala	Thr	Leu	Lys	Val	Ile	Asn	Glu	Pro	Gly	Glu	Thr
			100					105					110		
Glu	Val	Phe	Met	Thr	Pro	Gln	Asp	Phe	Val	Arg	Ser	Ile	Thr	Pro	Asn
			115				120					125			
Glu	Lys	Gln	Pro	Glu	His	Leu	Gly	Leu	Asp	Gln	Tyr	Ile	Ile	Lys	Arg
			130				135				140				
Phe	Asp	Gly	Lys	Lys	Ile	Ala	Gln	Glu	Arg	Glu	Lys	Phe	Ala	Asp	Glu

145 150 155 160  
 Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser  
 165 170 175  
 Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe  
 180 185 190  
 Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp  
 195 200 205  
 Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser  
 210 215 220  
 Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys  
 225 230 235 240  
 Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu  
 245 250 255  
 Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu  
 260 265 270  
 Gln His Asp Val Leu Lys Leu Glu Phe Glu Arg His Asp Pro Val Asp  
 275 280 285  
 Gly Arg Ile Ser Glu Arg Gln Phe Gly Gly Met Leu Leu Ala Tyr Ser  
 290 295 300  
 Gly Val Gln Ser Lys Lys Leu Thr Ala Met Gln Arg Gln Leu Lys Lys  
 305 310 315 320  
 His Phe Lys Asp Gly Lys Gly Leu Thr Phe Gln Glu Val Glu Asn Phe  
 325 330 335  
 Phe Asp Phe Leu Lys Asn Ile Asn Asp Val Asp Thr Ala Leu Ser Phe  
 340 345 350  
 Tyr His Met Ala Gly Ala Ser Leu Asp Lys Val Thr Met Gln Gln Val  
 355 360 365  
 Ala Arg Thr Val Ala Lys Val Glu Leu Ser Asp His Val Cys Asp Val  
 370 375 380  
 Val Phe Ala Leu Phe Asp Cys Asp Gly Asn Gly Glu Leu Ser Asn Lys  
 385 390 395 400  
 Glu Phe Val Ser Ile Met Lys Gln Arg Leu Met Arg Gly Leu Glu Lys  
 405 410 415  
 Pro Lys Asp Met Gly Phe Thr Arg Leu Met Gln Ala Met Trp Lys Cys  
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 Ala Gln Glu Thr Ala Trp Asp Phe Ala Leu Pro Lys  
 435 440

<210> 407  
 <211> 53  
 <212> PRT  
 <213> Mouse

<400> 407  
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 Val Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro Phe Pro  
 20 25 30  
 Leu Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys Gln Trp  
 35 40 45  
 Glu Gly Ser Thr Met  
 50

<210> 408  
 <211> 119  
 <212> PRT  
 <213> Rat

<400> 408  
 Gly Thr Ser Pro Ala Ser Val Leu Arg Ser Val Ser Ser Asp Pro Ser  
 1 5 10 15

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 Ala Ala Cys Gly Ile Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile  
                   35                                  40                                  45  
 Met Leu Gly Ile Phe Phe Asn Val His Ser Ala Val Leu Ile Glu Asp  
                   50                                  55                                  60  
 Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr  
                   65                                  70                                  75                                  80  
 Asn Leu Tyr Glu Gln Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu  
                                   85                                  90                                  95  
 Tyr Leu Leu Leu Gly Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys  
                                   100                                  105                                  110  
 Arg Lys Glu Tyr Met Val Arg  
                   115

&lt;210&gt; 409

&lt;211&gt; 590

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 409

Lys Val Glu Gly Glu Gly Arg Gly Arg Trp Ala Leu Gly Leu Leu Arg  
   1                                  5                                  10                                  15  
 Thr Phe Asp Ala Gly Glu Phe Ala Gly Trp Glu Lys Val Gly Ser Gly  
                   20                                  25                                  30  
 Gly Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp  
                   35                                  40                                  45  
 Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg  
                   50                                  55                                  60  
 Met Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg  
                   65                                  70                                  75                                  80  
 Tyr Ile Leu Pro Val Tyr Gly Ile Cys Gln Glu Pro Val Gly Leu Val  
                                   85                                  90                                  95  
 Met Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu  
                                   100                                  105                                  110  
 Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val  
                   115                                  120                                  125  
 Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp  
                   130                                  135                                  140  
 Leu Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr His Val Lys Ile  
                   145                                  150                                  155                                  160  
 Ser Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His Asp  
                                   165                                  170                                  175  
 Leu Ser Met Asp Gly Leu Phe Gly Thr Ile Ala Tyr Leu Pro Pro Glu  
                                   180                                  185                                  190  
 Arg Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val Tyr  
                   195                                  200                                  205  
 Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Lys Lys Pro Phe  
                   210                                  215                                  220  
 Ala Asp Glu Lys Asn Ile Leu His Ile Met Met Lys Val Val Lys Gly  
                   225                                  230                                  235                                  240  
 His Arg Pro Glu Leu Pro Pro Ile Cys Arg Pro Arg Pro Arg Ala Cys  
                                   245                                  250                                  255  
 Ala Ser Leu Ile Gly Ile Met Gln Arg Cys Trp His Ala Asp Pro Gln  
                   260                                  265                                  270  
 Val Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu Cys  
                   275                                  280                                  285  
 Glu Lys Pro Asp Glu Glu Val Lys Asp Leu Ala His Glu Pro Gly Glu  
                   290                                  295                                  300  
 Lys Ser Ser Leu Glu Ser Lys Ser Glu Ala Arg Pro Glu Ser Ser Arg  
                   305                                  310                                  315                                  320

Leu Lys Arg Ala Ser Ala Pro Pro Phe Asp Asn Asp Cys Ser Leu Ser  
 325 330 335  
 Glu Leu Leu Ser Gln Leu Asp Ser Gly Ile Ser Gln Thr Leu Glu Gly  
 340 345 350  
 Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Cys Lys Leu Pro Ser Ser  
 355 360 365  
 Ser Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser Ala Phe  
 370 375 380  
 Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg Glu Ala Ser Thr  
 385 390 395 400  
 Gly Asp Leu Gly Pro Thr Asp Ile Gln Lys Lys Lys Leu Val Asp Ala  
 405 410 415  
 Ile Ile Ser Gly Asp Thr Ser Arg Leu Met Lys Ile Leu Gln Pro Gln  
 420 425 430  
 Asp Val Asp Leu Val Leu Asp Ser Ser Ala Ser Leu Leu His Leu Ala  
 435 440 445  
 Val Glu Ala Gly Gln Glu Glu Cys Val Lys Trp Leu Leu Leu Asn Asn  
 450 455 460  
 Ala Asn Pro Asn Leu Thr Asn Arg Lys Gly Ser Thr Pro Leu His Met  
 465 470 475 480  
 Ala Val Glu Arg Lys Gly Arg Gly Ile Val Glu Leu Leu Leu Ala Arg  
 485 490 495  
 Lys Thr Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Ala Leu His  
 500 505 510  
 Phe Ala Ala Gln Asn Gly Asp Glu Ala Ser Thr Arg Leu Leu Leu Glu  
 515 520 525  
 Lys Asn Ala Ser Val Asn Glu Val Asp Phe Glu Gly Arg Thr Pro Met  
 530 535 540  
 His Val Ala Cys Gln His Gly Gln Glu Asn Ile Val Arg Thr Leu Leu  
 545 550 555 560  
 Arg Arg Gly Val Asp Val Gly Leu Gln Gly Lys Asp Ala Trp Leu Pro  
 565 570 575  
 Leu His Tyr Ala Ala Trp Gln Gly His Leu Pro Ile Gly Lys  
 580 585 590

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/NZ 99/00051

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
Int Cl <sup>6</sup> : C12N 15/12, 15/18, 15/19		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) C12N 15/12, 15/18, 15/19		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) GenBank, GenBank (ESTs), EMBL, EMBL (ESTs), SwissProt, TREMBL, PIR.		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GenBank (ESTs) Accession no AI412233	SEQ ID NO 119 Claims 1-17, 19, 21, 23, 25, 27, 28
X	GenBank (ESTs) Accession noAA850731	SEQ ID NO 119 Claims 1-17, 19, 21, 23, 25, 27, 28
X	GenBank (ESTs) Accession no AI299847	SEQ ID NO 119 Claims 1-17, 19, 21, 23, 25, 27, 28
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input type="checkbox"/> See patent family annex		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 8 September 1999		Date of mailing of the international search report 15 SEP 1999
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No.: (02) 6285 3929		Authorized officer  GILLIAN ALLEN Telephone No.: (02) 6283 2266

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/NZ 99/00051

**Box 1** Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-28  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
It is not economically feasible to carry out a full search on all sequences of the claims. Search has been limited to sequences from each of the Examples, namely: -  
SEQ ID NOs 68, 118 and 196 from Example 3; SEQ ID NOs 119 and 197 from Example 5; SEQ ID NOs 263, 270 and 344 from Example 5; SEQ ID NOs 273 and 347 from Example 6; SEQ ID NO 129 from Example 7
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

**Box II** Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/NZ 99/00051

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GenBank (ESTs) Accession noW97325	SEQ ID NO 263 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AA111146	SEQ ID NO 263 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AI037414	SEQ ID NO 263 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AI282114	SEQ ID NO 270 Claim nos Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AA865643	SEQ ID NO270 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AI140104	SEQ ID NO270 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AA726580	SEQ ID NO 273 Claim nos1-9, 11, 17, 19, 21, 23, 25, 27
X	GenBank (ESTs) Accession no AA407924	SEQ ID NO 273 Claim nos1-9, 11, 17, 19, 21, 23, 25, 27
X	GenBank (ESTs) Accession no AA498629	SEQ ID NO 273 Claim nos1-9, 11, 17, 19, 21, 23, 25, 27